



PHD

Designing An Educational Intervention For Crack Users Depending On Pharmaceutical Analysis Results

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**Designing An Educational Intervention For Crack Users
Depending On Pharmaceutical Analysis Results**

Mohammad Zaher Shehab

A thesis submitted for the degree of Doctor of Philosophy

University of Bath

Department of Pharmacy and Pharmacology

2014

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Summary/Abstract

Street-seized crack cocaine samples are cut with diverse impurities which may be very harmful to health. Harm reduction experts say that interventions are urgently needed to reduce the harmful behaviours associated with drug abuse. In this multidisciplinary approach, a successful intervention, Promoting Inhaled Pleasure Easily and Safely (PIPES), has been designed and tested in pilot studies. PIPES informs crack smokers about the crack sample content, efficiency of crack delivery, and the harms associated with different home-made smoking tools and cutting agents.

Crack samples were profiled by spectroscopic and chromatographic methods. In an attempt to track crack sources, PCA of the ^1H NMR spectroscopic data clustered samples of similar contents together. A laboratory crack smoking model was optimised to measure the emitted and recovered doses of cocaine and cutting agents from common crack smoking devices. Seized samples contained 24% cocaine base and 32% phenacetin. A medical inhaler delivered the highest dose of cocaine and phenacetin into the apparatus, then a glass pipe (shooter), and then tin cans.

The analytical results and the harms associated with each smoking device and toxic phenacetin were used to design PIPES, an educational intervention that was delivered by harm reduction workers to crack smokers. Users showed: a lack of knowledge of cutting agents and the harms associated with different pipes and cutting agents, their reasons for sharing pipes, and their attitudes to share knowledge and receive more information about cutting agents and pipes. The results of this applied research should be more widely known and used.

Acknowledgements

Completing my PhD degree may be the most challenging experience of the first 31 years of my life. The best and hardest memories of my doctoral journey are shared with many dear people.

First of all, I dedicate my thesis to my mother's soul who was waiting for me to come back with my degree and also to my brother's soul. I missed our last farewell ... to my family martyrs and to free Syrians martyrs.

I express my sincere thanks to my dear father who has given me his life for me to be what I am now. I would like to be able to compensate him at least a little bit compared with what he has done for me and my brothers and sisters. I thank my brother and sisters who supported me and encouraged me to keep going in the hard times during my PhD. Also, I cannot thank my beloved wife enough for encouraging me throughout this experience, and to her family for their caring and support. In my home country, I would like to thank all my teachers, staff, and friends who helped and supported me.

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List of Abbreviations

| | |
|----------------------|---|
| ¹ H NMR | Proton Nuclear Magnetic Resonance spectroscopy |
| 2D NMR | Two-dimensional Nuclear Magnetic Resonance spectroscopy |
| ACI | Andersen Cascade Impactor |
| AEME | Anhydroecgonine methyl ester |
| AIDS | Acquired immunodeficiency syndrome |
| ARA | Addiction Recovery Agency |
| AUC | Area under the curve |
| B20 | Bristol group (20 participants) |
| BBB | Blood-brain barrier |
| BBV | Blood-borne virus |
| BDP | Bristol Drug Project |
| BSDAS | Bristol Specialist Drug and Alcohol Service |
| BSE | Breast Self-Examination |
| CDSA | Controlled Drugs and Substances Act |
| CNS | Central nervous system |
| d ₆ -DMSO | Deuteriated dimethyl sulfoxide |
| DCM | Dichloromethane |
| DHI | Developing Health and Independence |
| DSC | Differential Scanning Calorimetry |
| DTA | Differential thermal analysis |
| EMCDDA | European Monitoring Centre for Drugs and Drug Addiction |
| ESI | Electrospray Ionization |
| ESI-MS | Electrospray ionization ion trap mass spectrometry |
| FT-IR | Infra-red spectroscopy |
| GC/FID | Gas chromatography/flame ionisation detection |
| GC-IRMS | Gas chromatography –isotope ratio mass spectrometry |
| GC-MS | Gas chromatography–mass spectrometry |
| HBM | Health Belief Model |
| HCA | Hierarchical cluster analysis |
| HCV | Hepatitis C virus |
| HIV | Human immunodeficiency virus |

| | |
|-----------|---|
| HPLC | High Performance Liquid Chromatography |
| HPTLC | High Performance Thin Layer Chromatography |
| HR | Harm reduction |
| HR ESI MS | High resolution electrospray ionisation mass spectrometry |
| HSQC | Heteronuclear Single Quantum Coherence |
| IDUs | Injecting drug users |
| IMB | Information Motivation Behavioural |
| IS | Internal standard |
| MRC | Medical Research Council |
| MS | Mass Spectrometry |
| N07 | Nottingham group (7 participants) |
| NEP | Needle exchange program |
| NMR | Nuclear Magnetic Resonance |
| NNEF | National Needle Exchange Forum |
| NSP | Needle and syringe program |
| PAP | <i>p</i> -aminophenol |
| PCA | Principal component analysis |
| PIPES | Promoting Inhaled Pleasure Easily and Safely |
| PLS | Partial Least Squares |
| REACH | Research Ethics Approval Committee for Health |
| ROAD | Recovery Orientated Alcohol and Drugs Service |
| RSD | Relative standard deviation |
| SCORE | Safer Crack Outreach, Research and Education |
| SCT | Social Cognitive Theory |
| SCUC | Safer Crack Use Coalition |
| SD | Standard deviation |
| SLT | Social Learning Theory |
| TB | Tuberculosis |
| TG | Thermal gravimetric |
| TPB | Theory of Planned Behaviour |
| TRA | Theory of Reasoned Action |
| UNODC | United Nations Office of Drugs and Crime |
| VSSC | Voltage-sensitive sodium channels |

Chapter 1

General Introduction and Aims

1.1. Introduction

1.1.1. Cocaine around the world

1.1.1.1. Coca leaf and cocaine

Cocaine is an active sympathomimetic drug isolated from the leaves of coca plants that are native to South America and are now typically grown in Colombia, Peru, and Bolivia (Fig. 1.1) [1]. Shrubs of the Erythroxylaceae (Fig. 1.2), namely *Erythroxylum coca* (Bolivian or Huanuco) and *Erythroxylum truxillense* (Peruvian or truxillo), are the source of coca leaves (Fig. 1.3) from which cocaine originates.



http://www.unodc.org/documents/wdr/WDR_2009/WDR2009_Coca_Cocain_Market.pdf

Fig. 1.1. Geographical distribution of coca shrubs (accessed 31.08.2014) (with permission).

Coca has been used as a traditional drug in South America for thousands of years. It is used either as a general stimulant or for some limited medicinal usage [2]. Early explorers brought back this plant to Europe; scientific studies and medical involvement started in the 19th Century [3]. In the late 19th Century, coca extract and cocaine were prepared as remedies for many problems. When its dangers became known and clear alternatives became available, its legal medical use decreased [2].



Fig. 1.2. *Erythroxylum coca* LAM. Schopke T. 2011. Available from:

<http://sarcozona.org/wp-content/uploads/2011/05/020912021.jpg> (accessed 31.08.14).



Fig. 1.3. Leaves of a coca plant, UNODC, World Drug Report, 2011 (with permission).

The total alkaloids isolated are ~0.7-1.0 % of coca leaves. There are different methods to extract the crude alkaloids from the coca leaves. They can be treated with dilute sulfuric acid to form the sulfate salt or with lime (CaO) and petroleum or other organic solvents to yield the free-base form [1]. Cocaine is a tropane alkaloid, as are the hydroxy-acid ecgonine, and the axially orientated atropine (Fig. 1.4)

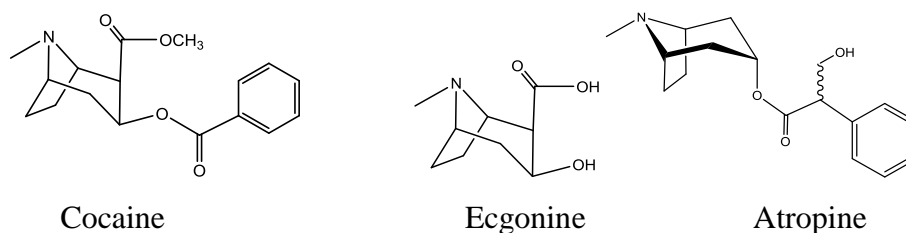


Fig. 1.4. Alkaloids based on the tropane ring.

1.1.1.2. Production of cocaine

The illicit production of cocaine paste, free-base, and HCl salt includes three steps: extraction of coca paste from coca leaves, purification of coca paste to cocaine free-base, and then conversion of the base into cocaine hydrochloride. This method accounts for more than 99.99 % of all illicit cocaine seized [4]. The differentiation of illicit/licit for illicit natural, illicit synthetic, and pharmaceutical cocaine typically follows the purity of the samples. Even unadulterated cocaine contains numerous impurities. Chromatographic methods are used for the alkaloid analysis of coca leaves and for the characterization of alkaloidal impurities and manufacturing by-products in illicit refined cocaine samples [5].

Cocaine usage and abuse is an immense problem. The global problems of cocaine prevalence, health, social and economic problems are discussed in their three principal dimensions: production, trafficking, and consumption [6]. According to the United Nations Office of Drugs and Crime (UNODC) annual World Drug Reports, cocaine is the second largest illicit drug in manufacture worldwide after cannabis. Although over the period 2007-2009, a clear decrease was apparent in both opium and cocaine production (about 21% for opium and 13% for cocaine).

The three Andean countries (Colombia, Peru, and Bolivia, Fig. 1.1) are the producers of cocaine. Cocaine trafficking occurs with both intra- and inter-regional patterns (Fig. 1.5). Although the importance of North America has decreased as a main cocaine consumer since 2009, West and Central Europe are the next main terminals either by direct shipments or exported via African countries. Also noticed was an increase in trafficking cocaine towards east Asia [6]. Cocaine is trafficked by sea and by air. Cocaine trafficking increased sharply between 1998-2006, then it decreased heavily between 2006-2009, partly due to the improved cooperation with Latin American law enforcement counterparts to share information to seize cocaine in South America instead of waiting for the cocaine to arrive in Europe [6].

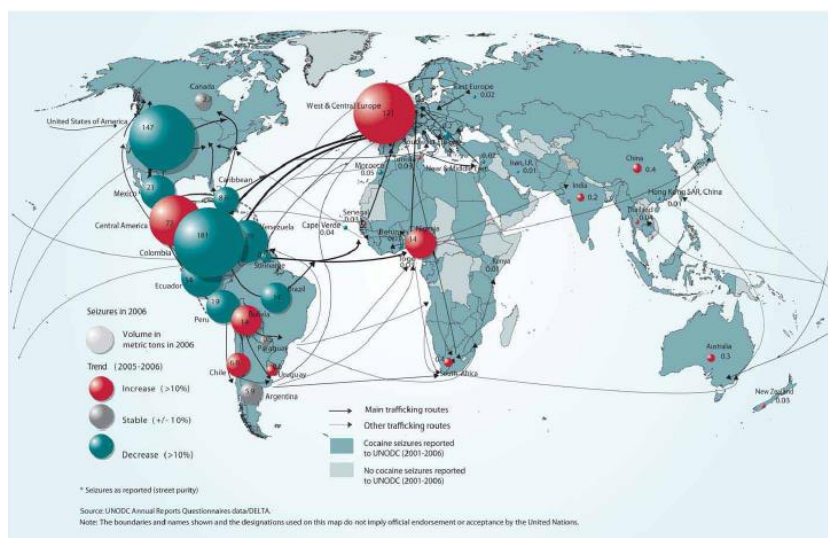


Fig. 1.5. Trafficking in cocaine, 2006 (from [7] with permission).

http://www.unodc.org/documents/wdr/WDR_2008/WDR_2008_eng_web.pdf

World Drug Report, page 15 (accessed 31.08.14).

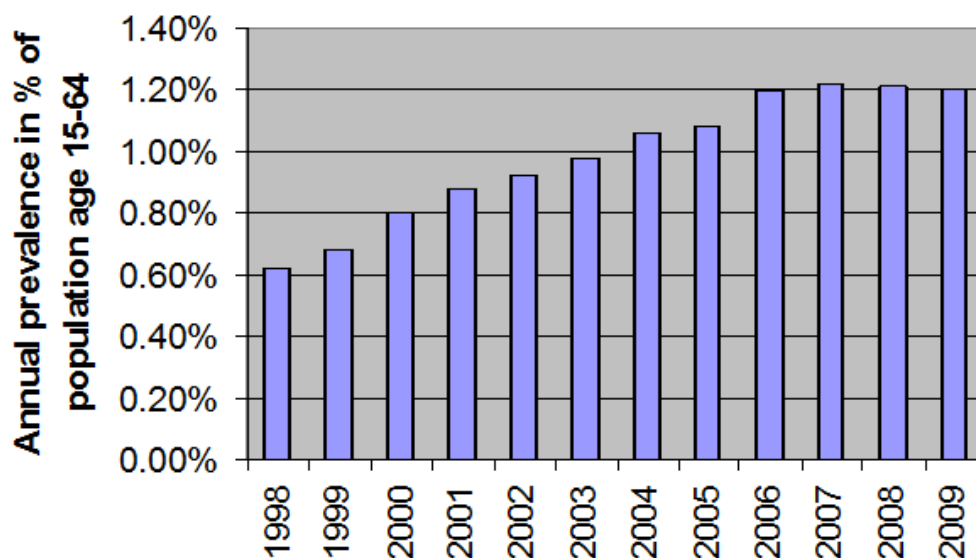


Fig. 1.6. Annual prevalence of cocaine use among EU and EFTA countries, 1998-2009 (data taken from [6]).

Cocaine is the second most prevalent drug in Europe with 4.30-4.75 million users. A UNODC report [6] shows that 30 % of global cocaine users are found in Europe, and 90 % of them are located in West and Central Europe where cocaine prevalence rates doubled between 1998 and 2006, but then stayed constant between 2006 and 2009 (Fig. 1.6) [6]. Overall cocaine levels in the EU/EFTA area were 1.2 % in 2009 (Fig. 1.6) [3]. Cocaine users are concentrated in three countries, the United

Kingdom (Fig. 1.7), Spain, and Italy. These account for two thirds of all cocaine users in Europe [3]. Globally, between 149-272 million people (3.3-6.1 %) aged 15-64 years have used illicit substances at least once in the previous year as evaluated by UNODC. Concerning cocaine consumption, it is ranked fourth in terms of universal popularity, with ratings ranging between 14-21 million people (0.3-0.5 %) aged 15-64 years [6]. European and regional drug trends and patterns are different from the global trends with an emphasis on consumption rather than production [6].

1.1.1.3. Cocaine use/market changes during the last 10 years

For a lot of cocaine users, crack cocaine became the most common form in the 1980s [8, 9]. In 2011, the United Nations report classified cocaine as the second most problematic drug after heroin regarding harmful health effects [6].

Although many studies show that crack use is increasing, the attention directed toward this use (i.e. smoking crack) is still negligible compared with the attention given to drug use by injection [10]. In Canada, different studies suggest that between 50-80 % of drug users have used crack recently [10].

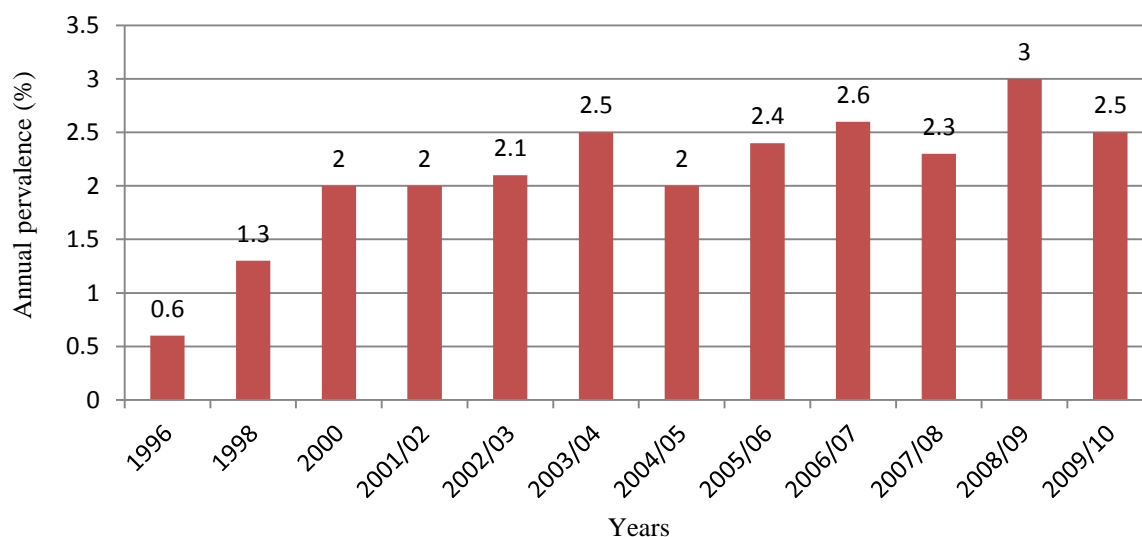


Fig. 1.7. Trends in annual prevalence of cocaine use in England and Wales (UK): 1996-2009/10 (data taken from [6]).

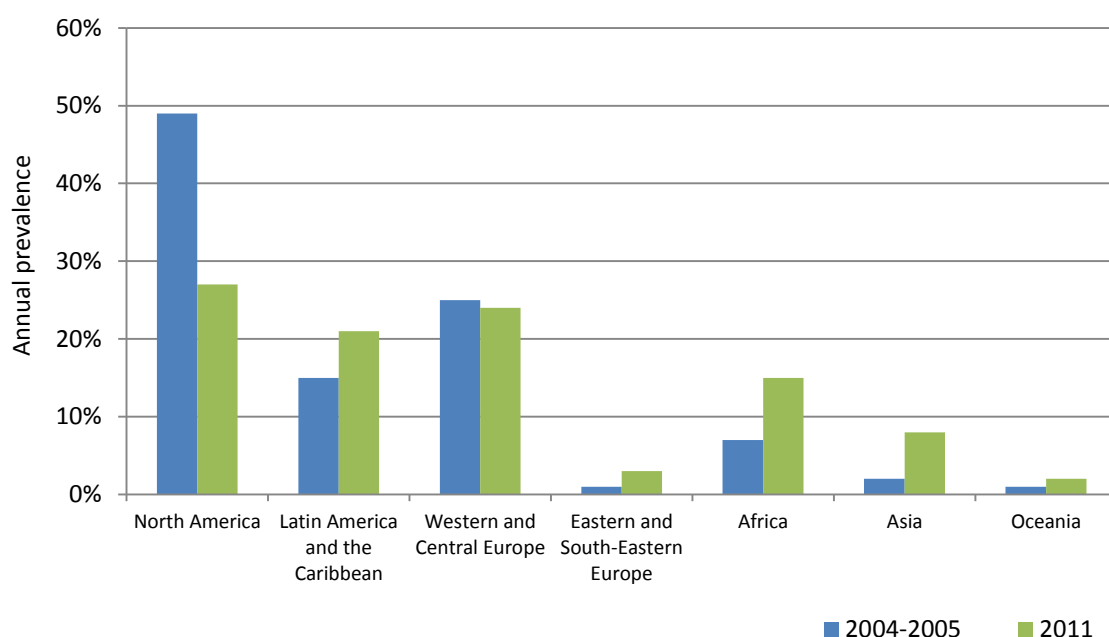


Fig. 1.8. Distribution of cocaine users (annual prevalence), 2011 data compared with data for the period 2004-2005 (data taken from [11]).

An increase in prevalence was noted in regions of huge population such as South America, Asia, and Africa [11]. Fig. 1.8 compares the annual prevalence of cocaine users between 2011 and the period 2004-2005 in different regions around the world.

The data show that in England and Wales cocaine use trebled between 1996-2000 (Fig. 1.7). The prevalence of cocaine use during the first 10 years of the 21st century showed a fluctuation with a slight overall increase between 2000-2010. Most countries in Europe and in South and Central America reported a stable trend in cocaine use, while cocaine use decreased in North America which is considered to be the area of highest consumption in the world. The reason for this decrease in North America is due to a reduction in the amount of cocaine trafficked via Mexico and also the price of cocaine rising by more than 80 % between 2006-2009 (Fig. 1.9).

At the same time as the decrease of cocaine use in North America, reports indicated an increase in cocaine use in Western Europe and, concomitantly with this increase, a decrease in the price of cocaine was observed between 1990-2007 (Fig. 1.9). Fig. 1.10 shows the differences between the prices of cocaine in Western Europe between 1990-2007 at two levels, retail and wholesale prices [12].

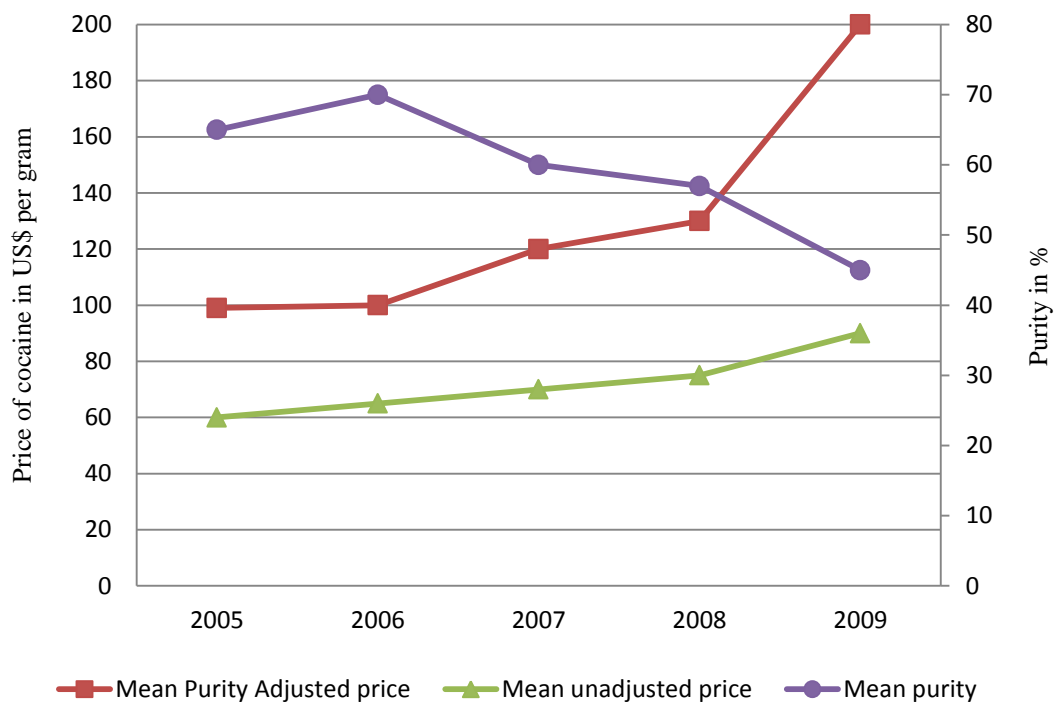


Fig. 1.9. USA, cocaine price and purity (data taken from [12]).

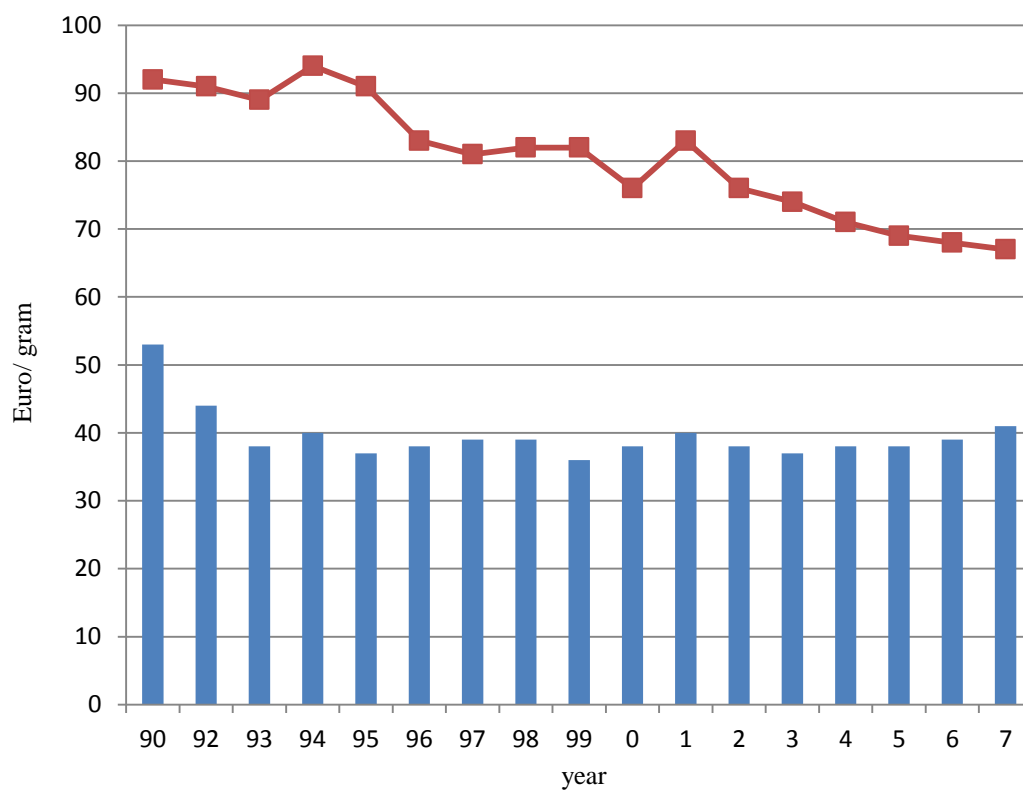
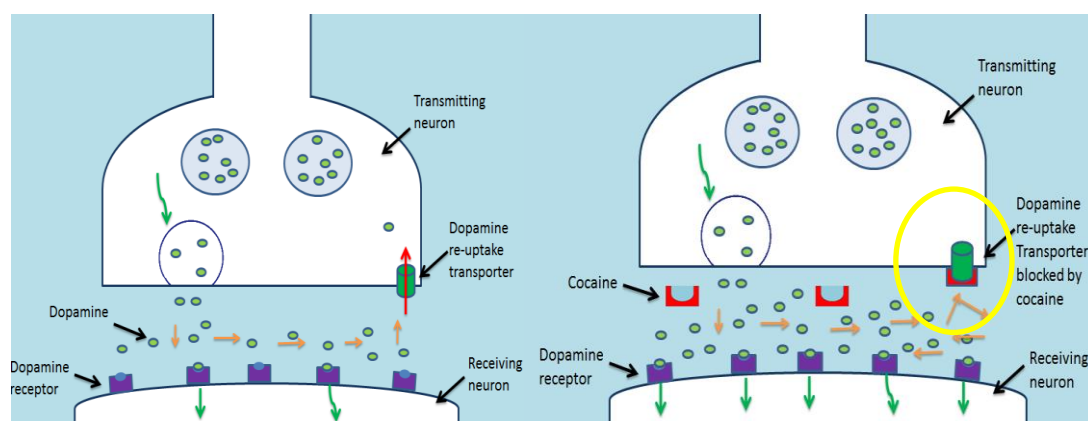


Fig. 1.10. Western Europe, cocaine retail and wholesale prices, 1990-2007, €/gram (data taken from [12]).

1.1.2. Cocaine pharmacology

Cocaine acts as a local anaesthetic by blockage of voltage-sensitive sodium channels (VSSC). In addition to blocking Na^+ channels, it also blocks K^+ channels and this may cause cardiac arrhythmias. Cocaine is the only local anesthetic that causes vasoconstriction. This property is responsible for the necrosis and perforation of the nasal septum noticed with the long-term administration of cocaine leading to accumulation of norepinephrine in the synaptic cleft [13]. Cocaine binds to the dopamine re-uptake transporter on pre-synaptic membranes and causes overstimulation at dopaminergic synapses in the brain (Fig. 1.11). The replacement of dopamine from the synaptic cleft and its subsequent degradation by monoamine oxidase in the nerve terminal is obstructed by cocaine binding, resulting in further nerve impulses. A feeling of euphoria is produced by the augmented energizing of the dopaminergic reward pathway [14]. Ultimately however, dopamine is depleted by prolonged intake of cocaine leading to severe depression [13]. Cocaine stimulates the central nervous system (CNS) causing agitation, dilated pupils, tachycardia, hypertension, hypertonia, hyperreflexia, and hallucinations. Convulsions, coma, and metabolic acidosis may develop. Symptoms of CNS stimulation and sympathetic over-activity are very marked in cocaine overdose. A single oral dose of 1 g may be fatal, but some people have a cocaine hyper-sensitivity, and severe toxicity may occur after doses of only 10 mg intravenously. Systemic absorption of small doses may slow the heart, but with increasing doses tachycardia, hypertension, and ventricular fibrillation occur [2].



(accessed 02.03.14) (with permission).

Smoking crack cocaine causes many pulmonary symptoms, e.g. pulmonary oedema, hypersensitivity pneumonitis, pulmonary haemorrhage; other routes of cocaine abuse do not cause these pulmonary problems [15]. Topical application of

cocaine to the cornea can cause corneal damage with clouding, pitting, sloughing, and occasionally ulceration. Topical application to the nose or mouth has been reported to cause loss of smell and taste respectively [14].

1.1.3. Cocaine metabolism

Plasma butyrylcholinesterase and hepatic carboxyesterase metabolize cocaine rapidly into ecgonine (see Fig. 1.4) and its corresponding methyl ester. Spontaneous hydrolysis of the methyl ester may produce benzoylecgonine which is another cocaine metabolite. Cocaine and its metabolites are mainly eliminated in urine, with ~10 % appearing as the unchanged drug [14]. Cocaine gathers in the CNS, crosses the blood-brain barrier (BBB), also crosses the placenta, and is secreted in breast milk [14].

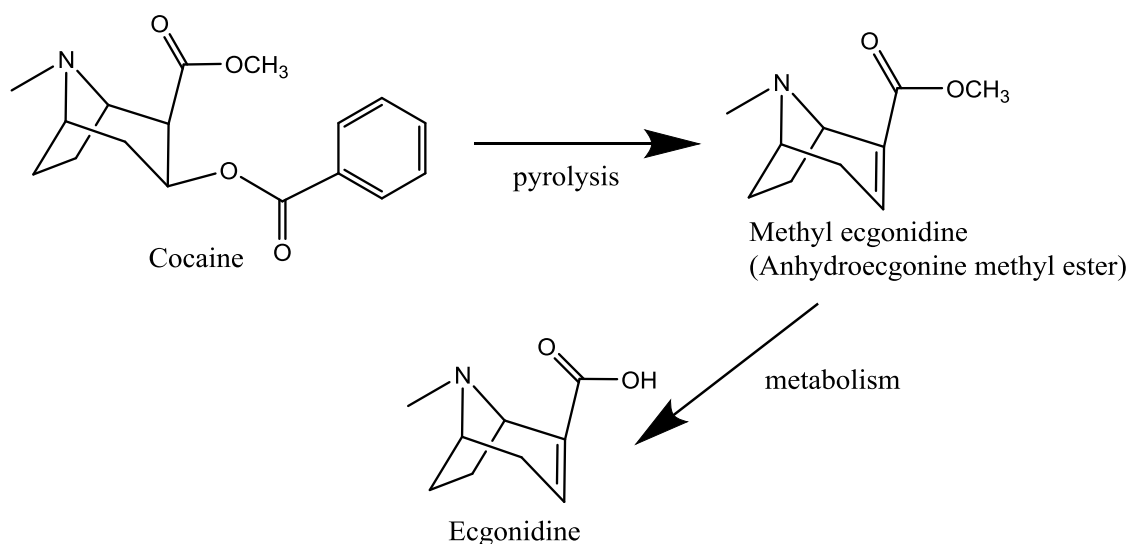


Fig. 1.12. Conversion of cocaine into methyl ecgonidine and ecgonidine [16].

Smoking cocaine free-base produces other compounds which are markers in forensic analysis. Methyl ecgonidine (anhydroecgonine methyl ester) is the pyrolysed compound obtained by heating cocaine free-base (Fig. 1.12). Butyrylcholinesterase activity metabolizes methyl ecgonidine to the free acid ecgonidine (Fig. 1.12). Ecgonidine is a longer remaining marker of crack cocaine having been smoked than is its corresponding methyl ester [16].

1.1.4. Adulterants identified in cocaine

Illicit drugs samples may contain additional substances besides the active drug. These adulterants can themselves cause harmful side-effects, even as far as causing early death [17]. The substances added to cocaine and crack samples have changed over the past 30 years. The first detected adulterants in cocaine in the 1980s were lidocaine and sugars. Caffeine was identified during the 1990s. After 2000, it was shown, from seized cocaine samples, that phenacetin became more frequent as a major adulterant [17]. Cutting agents are usually added to increase the bulk of drug samples to get more profits, or to increase the drug effects, or to mimic the drug effects by incorporating cheaper materials [18].

According to the European Monitoring Centre for Drugs and Drug Addiction (EMCDDA) reports, the purity of cocaine samples in Western Europe declined between 2002-2007 when the mean range of the purity was 22-57 %. Also, a massive adulteration of cocaine in England and Wales in 2008 could explain the decline in the purity of seized cocaine samples from 63% at importation to 29% at street level during the same period [17]. There are different expressions which are used to characterise the substances added to illicit drugs. The three most used expressions [17] are:

- By-products from the preparation methods are referred to as Contaminants.
- Pharmacologically active substances added to afford either synergistic effects or to counter side-effects are referred to as Adulterants.
- Inert ingredients added to increase the bulk of samples and reduce the amount of active drug are referred to as Diluents [17].

Cocaine street samples are usually cut by dealers with diluents or/and adulterants. Diluents, pharmacologically inert substances such as sugars, talc, and corn starch, are added to increase the samples' bulk and dealer's profits. Adulterants, pharmacologically active substances, are added by dealers to amplify the wanted effects of the illicit substances [6].

Cocaine adulterants (Table 1.1) can be divided into three main categories: local anaesthetics, stimulants, and toxic chemicals. The purpose of adding local anaesthetics to cocaine is to simulate the anaesthetic properties of cocaine. They are considered the third most common cocaine adulterants. Stimulants such as caffeine (Fig. 1.13) mimic cocaine effects and are legally available in pharmacies in the UK.

Table 1.1

Adverse effects of cocaine adulterants (data taken from [19]).

| Adulterant | Pharmacology | Adverse effects |
|------------|--|---|
| benzocaine | local anaesthetic | methaemoglobinemia is associated with large doses, CNS: nausea, vomiting, dizziness, tremors, convulsions Cardiovascular: myocardial depression, hypotension, bradycardia, arrhythmias |
| caffeine | stimulant | Chronic use associated with withdrawal symptoms, including headache, irritability |
| levamisole | anti-parasitic agent, colon cancer and rheumatoid arthritis [16] | After acute intake: nausea, diarrhoea and dizziness After prolonged intake: muscle pain, headache, fever, insomnia, dizziness and convulsions |
| lidocaine | local anaesthetics, similar anaesthetic effects to cocaine | Central nervous system (CNS): nausea, vomiting, dizziness, tremors, convulsions. Cardiovascular: myocardial depression, hypotension, bradycardia, arrhythmias |
| phenacetin | painkiller related to paracetamol | Chronic use associated with nephrotoxicity leading to incontinence and back and flank pain. Bladder cancer [17]. |
| procaine | local anaesthetic | CNS: nausea, vomiting, dizziness, tremors, convulsions Cardiovascular: myocardial depression, hypotension, bradycardia, arrhythmias |

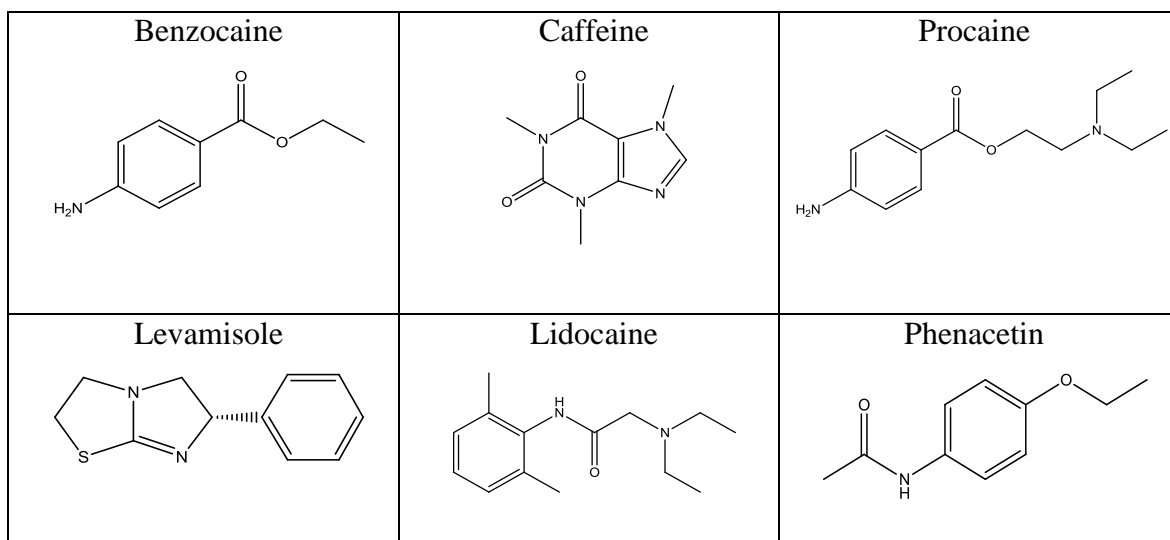


Fig. 1.13. Common cocaine adulterants.

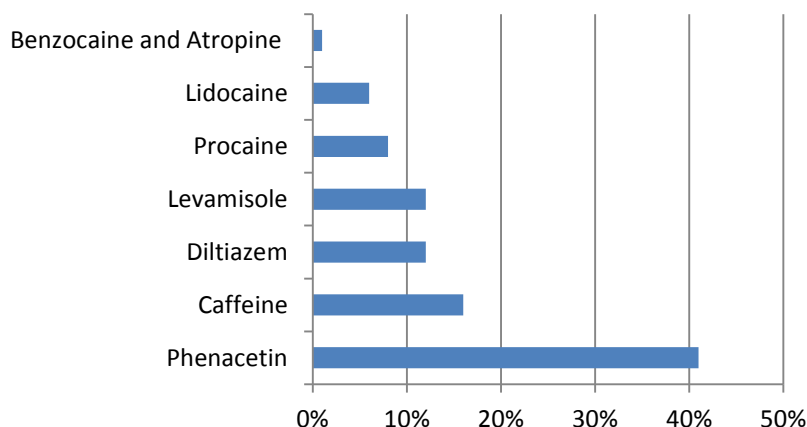


Fig. 1.14. Percentages of the identified adulterants in Dutch cocaine samples (1999-2007) (data taken from [19]).

Levamisole (Fig. 1.13) was reported in up to 70 % of analysed cocaine samples in the USA and Europe, it is an anti-parasitic agent and also used to treat colon cancer and rheumatoid arthritis [5, 6]. Levamisole is cheap, available, and it is unnoticed by cocaine users due to its appropriate look, taste, and even melting point. It was found that levamisole had the same symptoms of heroin withdrawal and increased the levels of different chemicals in the brain. This suggests that it may change the metabolism of dopamine and so it has the ability to increase cocaine effects [20, 21]. In 2009, Brunt and colleagues reported [19] the diversity among the most common adulterants in cocaine samples in the Netherlands during 1999-2007 (Fig. 1.14). This reveals that phenacetin became the most common adulterant, identified in more than 40 % of

cocaine samples, while other common adulterants were identified in 12-16 % of the samples [19].

The health consequences are not only related to the cocaine in the case of crack cocaine users. Many studies and reports reveal the toxicities and adverse effects of the identified cutting agents found in cocaine samples. Although there are many reasons behind adding each substance to the illicit drug, cocaine users consume the samples and they suffer from the harmful effects of all the ingredients in the formulation. One of the common adulterants in cocaine samples is phenacetin, an analgesic, but now withdrawn from the market due to its carcinogenic effects. Phenacetin was reported as a reason for acute intoxication of a 25 year old [22]. It is difficult to explain the cardiac and hallucinogenic effects associated with phenacetin. The assessed carcinogenic risk associated with phenacetin was from at least 0.5g of phenacetin daily; it is difficult to reach this dose normally. There are no reported studies evaluating the role of route of administration of phenacetin, if taken nasally it could increase the toxicity. There may even exist an interaction between cocaine or one of its metabolites with phenacetin. Although selling phenacetin is not allowed any more in many countries, it is still available worldwide. However, it is uncertain why it is used widely as a cutting agent in drugs [19]. Another case reported a methaemoglobinemia caused by taking street cocaine samples cut with benzocaine, a commonly used local anaesthetic [23, 24]. Moreover, harmful cases were reported when unknown, adulterated or fake samples were sold as cocaine [25]. Deaths connected with the use of illicit drugs may result from: suicide, fatal drug overdoses, accidents, deaths among injecting drug users (IDUs), and from infectious diseases e.g. human immunodeficiency virus (HIV) and hepatitis C virus (HCV) due to sharing equipment, medical conditions e.g. organ failure due to chronic drug use [6].

Many of those cases of harm to the users, but not harm caused by cocaine, could have been avoided by informing the drug users what their samples actually included. Such information and advice for drug users about the content and adverse effects rely on the results of analytical profiling techniques. Such profiling techniques may use chromatographic or spectroscopic methods, or most likely both, to provide data about the street samples' content. There are supportive strategies that aim to reduce the harmful effects associated with the drug, e.g. harm reduction (HR) interventions. Not only harm related to the illicit drugs was reported [15], but also adverse effects of drug impurities were reported [19]. More HR interventions about the harm associated with

impure drug samples could help to reduce the number of cases. Especially cases which indicate hazardous outcomes from the toxic effects of cutting agents. The efficiency of the smoking paraphernalia varies depending on the quality of materials, especially in the case of handmade tools such as crack pipes where smokers can use the different available materials regardless of the effectiveness and safety of those pipes. Sharing equipment is considered to be one of the main routes for the transfer of viruses between drug users, e.g. sharing needles to inject drugs, or sharing a pipe between drug smokers (crack smokers in this case) where there is the risk of cuts or burns, and especially the risk of those then leading to the transfer of blood-borne viruses (BBV).

1.1.5. Harm reduction

Harm reduction (HR) is a series of principles giving rise to strategies that explore a relief of adverse effects of risky behaviours, e.g. alcohol abuse, drug use, unprotected sex. Many terms, e.g. damage limitation, casualty reduction, harm minimisation or risk reduction, have been used to describe the HR approach [26]. However, HR is focused on decreasing risks of abuse and the problems that accompany drug use. HR is an evolving program related to abused substances, HIV prevention and treatment interventions. The need for HR is rising due to the necessity of reacting to drug use more than by imprisonment and law enforcement to sort out the health, crime, and violence problems associated with drug abuse [27]. HR is based on a group of hypotheses and rules about how individuals may make alterations to their behaviours and life-style [27].

HR rules include realizing that the necessity of change must be established on an individual basis. However, low expectation strategies can be successful in achieving the required changes without any individual promise of abstinence from drugs. HR emphasises that people are the first agents in decreasing harm from their hazardous behaviours. It sets up the welfare and quality of life for both individuals and communities [27]. The primary goal is to reduce harm without necessarily, and depending on particular circumstances, seeking to reduce drug abuse. Long-term aims start from steps that can be relatively easily applied. The long-term aim for HR could be the route towards abstinence, which may be considered as an ideal outcome, but another alternative is to achieve a reduction in harm [27, 28].

1.1.5.1. Harm reduction principles

HR is an approach to avoiding health problems and encouraging healthier behaviours rather than taking judgmental decisions about what people should do related to their individual lifestyle and health. However, not everyone is ready or able to make decisions concerning stopping dangerous or illegal behaviours. For that reason, HR concentrates on supporting evidence-based methods of lessening health problems related to drug abuse. The methods to achieve these HR objectives rely on the following principles [29]:

1. Targeted at risks and harms: specific risky behaviour or health problems associated with drug abuse can be determined through finding the answers to the questions of what are the harms and risks? What are their causes? What can be done to minimize them?
2. Evidence-based evaluation and cost effectiveness of each method or procedure applied to alleviate the risky outcomes of drug use or serious behaviours.
3. Incremental: HR experts recognize the importance of any positive transformation in individuals' lives because HR contributions aim to achieve helpful steps at the individual or community levels. They may benefit more from small advances for many people than from big gains for a few. The most urgent HR priorities are to keep users alive and avoid unnecessary injuries.
4. Dignity and compassion: drug users should be accepted as they are, with consideration and fairness always included in language and vocabulary without any judgmental behaviour.
5. Universality and interdependence of rights: HR does not discriminate against people due to their drug using.
6. Challenging policies and practices that maximize harm: Many policies and practices, deliberately or not, create additional risks for drug users. HR has to assist drug users to improve their life individually, but it is necessary to address the prejudice against them that makes their environment more dangerous.
7. Transparency, accountability and participation: decisions affecting drug users and their communities should be made in cooperation with stakeholders.

HR as a grassroots campaign moved to many European countries during the 1980s and it influences the policies there. The central goal of HR is the belief in the

possibility to change the behaviour of drug users and the circumstances in which they practice their drug use to reduce various associated health problems. There are many HR interventions for drug use, e.g. needle exchange programs (NEPs), methadone maintenance, and safe-use educational activities. The educational campaign could show the HR strategy by highlighting the health benefits of some behaviour compared with a more risky one. This may end-up encouraging drug users to use a less harmful route of drug administration [30]. HR goals also include many more examples, e.g. learning safer practices of drug use, clean syringe use, being informed about overdose risks and prevention, converting to less risky and harmful substances [31].

Modifying the behaviour of drug users to reduce the risks associated with their drug-use patterns can employ different theories or models to determine health behaviours. One of these models is the Information Motivation Behavioural skills (IMB) model. IMB emphasizes the group of information, motivation, and behavioural skills factors related to practice health behaviours [32]. IMB was developed by Fisher and Fisher to determine the psychological elements of behaviours which have the ability to improve health behaviour. It was designed basing on the outcome of previous theories and to avoid the limitation of interventions applied to reduce HIV risks. Also, it was developed to form easily targeted intervention operations.

1.2. Aims

The aims of this thesis are to be achieved through using analytical techniques to identify cocaine, quantify its purity, and also determine the cutting agents added in manufacture or by drug dealers. ^1H NMR data will be used within statistical software (PCA) to attempt to track the channel of distribution and any common sources of seized crack cocaine samples. Additionally, as crack cocaine is used by volatilising it with various handmade devices, another aim is to design and develop a smoking model to measure the efficiency of those devices under simulated laboratory smoking conditions. The results of analytical profiling will then be used to design an educational intervention that will be delivered by harm reduction workers to crack cocaine smokers. This intervention will focus on increasing the knowledge and behavioural skills of crack abusers. Thus, this will be a pilot study of the impact of pharmaceutical analytical results about seized crack cocaine content and the different efficiencies of the used devices on smokers' behaviour aiming for harm reduction.

Those aims will be met through the following eight objectives:

1. A focused review of analytical cocaine profiling, thermal behaviour studies, and the tracking of sources by using analytical results.
2. Analysis of seized crack cocaine by spectroscopic and chromatographic methods to determine analytical profiles for those crack cocaine samples.
3. Application of PCA and HCA statistical methods to ^1H NMR spectroscopic data to attempt to track sources of the seized samples.
4. Thermal analysis studies of crack samples and comparison with authentic and physical mixtures of cocaine prepared with the same adulterants in the same ratios.
5. Design of a crack smoking model to evaluate the efficiency of the handmade devices used and identification of the by-products under crack smoking conditions.
6. Design of a questionnaire to measure the knowledge and motivation of crack smokers about cocaine impurities and their adverse impact on their health.
7. Use of the analytical results to design a harm reduction intervention which could lead to change the knowledge and awareness of crack smokers. This will be delivered to crack smokers by harm reduction workers.
8. Measurement of the components of an Information Motivation Behaviour skills model before and after the intervention to evaluate the impact of the intervention.

Chapter 2

Literature Review - Analytical aspect

Illicit drugs contain different groups of drugs from different sources and prepared by various methods. Characterization of drug samples can rely on more than one key component depending on the purpose and the samples analysed. The main key components that can be used in the characterization process are: firstly, in the case of plant-based drugs such as heroin, cocaine and cannabis, the natural compounds themselves. Secondly, the by-products may be produced during the preparation processes that are related to the methods of manufacture. Finally, one of the main key components is the cutting agents which may be added at different steps of preparation or distribution [33]. The chain of drug supply is complicated and not short, including the manufacturer, trafficker, distributor, and users. It is complex chain and process because each member in this chain can deal with more than one in lower and upper levels. This can make the tracking process is very difficult to find out the source of samples. Cutting agents can be added at any level of this chain [33].

Drug characterization/impurity profiling studies can serve different purposes, in particular, they may help to: (a) establish specific links between two or more samples that were seized from different areas to improve the information about drug traffic processes [34]; (b) identify the source depending on the similarities in the content; and (c) identify common cutting agents which may themselves cause harm to users. Those cutting agents can be related to the fluctuations in purity of drugs in drug markets and the reasons behind using specific agents [33, 35]. King has classified the reasons behind studying the purity of illicit drugs [36]. The reasons can be applied either to the drug provided as a powder or as tablets/capsules. He mentioned that the purity can provide information for different purposes: the most common reason to study the purity of illicit drugs through comparative studies is to provide information about any possible link between two or more samples. Moreover, the purity of illicit drugs is one of many factors that are used to gather various samples into groups. The idea of this clustering is that similar samples may come together in one group either they may be produced by the same clandestine chemist e.g. amphetamine [36, 37], or the samples may have the same geographical origin e.g. heroin [36, 38, 39], and cocaine [35]. Furthermore, a quantitative analytical aim is required in the case of cocaine (as free-

base) according to the Misuse of Drugs Act Regulations (1985). Characterization of drug sample may be defined as the physical and chemical identification and quantification of the major ingredients of a drug sample including the existence and type of cutting agents (adulterants and diluents). Impurity profiling utilises a range of different analytical techniques to present a full view (profile) of the drug sample [40].

The characterization of the samples can be carried out with chemical examination by analytical methods to identify every component in the analysed samples. The identifications can include the major, minor, and trace elements. Those tests can provide important explanations for the comparing different samples through impurity profiles [33].

One of the first cocaine profiling published studies was in 1991 by Casale and Waggoner [40, 41]. This paper was published at a time when cocaine abuse was one of epidemic proportions across all groups of society in the USA. The necessity for detailing the sample's signature was to give more evidence about sample sources [41]. They used chromatographic methods to identify different impurities from different sources e.g. impurities which were produced from extracted alkaloids and/or from the plant, solvents, packing materials [41].

One of the first researchers who studied cocaine samples and the profiling of cocaine for different purposes was Casale. This research concentrated on the detection and analysis of different impurities in cocaine samples. These impurities are naturally occurring or have arisen during cocaine manufacturing or in its isolation from coca leaves. Also, they studied the effect of UV radiation to which the plant was exposed on the components and the percentage of different compounds which exist naturally with cocaine. Casale and co-authors were interested in different analytical methods of cocaine and natural and synthesized impurities. They reported the isolation, detection and determination of cocaine, natural impurities and by-products [42].

Janzen and his colleagues analysed cocaine samples to establish a database depending on measuring different compounds such as natural alkaloids. In 1994, they reported [43, 44] the development of a rapid method to compare the concentration of cocaine content in samples to create a cocaine database. They used capillary gas chromatography and a nitrogen-phosphorus detector. The data collected were analysed by a multivariate statistical technique to reveal that the percentage content of four alkaloids (tropacocaine, norcocaine, *cis*-cinnamoylcocaine, and *trans*-

cinnamoylcocaine) were sufficient to discriminate cocaine samples from unrelated sources [43, 44].

Guthery [45] in 2010 attempted to develop a new method to isolate and detect more drugs, metabolites, and impurities using a two dimensional GC (GC×GC). 2D GC gives the choice to further analyse through a secondary column before passing the separated compounds into a mass spectrometer, providing a higher resolved chromatogram for complex samples compared with a 1D gas chromatogram. This can allow testing of a huge number of compounds in one experiment which may save time and laboratory work. This can help to identify more compounds especially where there are co-eluting matrix compounds as GC-MS is not effective enough to give highly resolved peaks. This method enabled the origin of naturally occurring cocaine to be distinguished from semi-synthetic cocaine depending on the nature of the impurities which exist naturally with cocaine. This method also solved one of most complicated problems in GC which is the broadening and tailing of peaks [45]. The above profiling studies aimed to find more evidence for investigation purposes to enable law enforcement authorities to discover the source or the link between different samples or batches.

Different illicit drugs (cocaine and heroin) were analysed to determine the cutting agents and the reasons behind some injuries associated with drug abuse. In 1984, Cunningham and co-workers analysed cocaine and heroin samples from different cities [46]. They identified eleven adulterants in the samples which were examined. Intravenous use of heroin and cocaine is linked with renal injuries. They analysed different samples of heroin (white, brown) and cocaine from different cities. It was clear that there was variety in the purity of the samples. They also noticed that some samples from certain cities contain a unique adulterant, while other samples contained other mixture of adulterants. Concerning the cocaine samples, they included different adulterants e.g. lidocaine, lactose, mannitol, inositol, dextrose. The lidocaine was found only in cocaine samples. The adulterants rather than the heroin or cocaine are more likely responsible for any kidney injury [46].

Bernardo and co-workers [47] studied cocaine samples in Brazil in 2003. They used a two-step analysis to identify the sample contents by TLC then quantified the compounds by GC-FID. The results of their analysis show that in 1985 the most common cocaine adulterant was lidocaine; by 1993 this adulterant had disappeared to be replaced by caffeine. They noticed that perlocaine was used in North America only.

The samples analysed revealed that the different patterns of adulteration were found in samples seized from different places. The massive fluctuation of street cocaine composition caused the unexpected impacts on drug users. Those impacts can range from CNS euphoria to fatal intoxication; the impact depends on the tolerance ability of users and the purity of samples. Additionally, the synergistic harmful effects of some adulterants such as the cardiotoxicity effects result from adulterating cocaine with lidocaine [47].

Eyanagi (1991) [48] evaluated the impact of *p*-aminophenol (PAP) the main metabolite of paracetamol and phenacetin on rats. The study discussed the effect of PAP through its ability to bind with glutathione and this reaction was carried out in rats. Their results explained PAP's nephrotoxic effects. This paper could give information about the results in the case of massive use of paracetamol or phenacetin as diluent in illicit drugs such as cocaine or heroin [48].

In 2009, Brunt et al. reported [19] the increase in demand for cocaine and other illicit drugs. It was noticed that diluents were used more and more. This study also analysed street cocaine samples to study the effects of diluents and cocaine together. They reported that many diverse effects are associated with the adulterated cocaine, and users suffer from more side effects than what is found to be the case when using unadulterated cocaine. During the years of study from 1999 to 2007, it was clear that the proportion of adulterated cocaine (6.5 % to 57 %), and the diversity of adulterants found in cocaine and their percentage increased, i.e. there were many new adulterants which were not found at the beginning of the study, e.g. benzocaine, hydroxyzine, and atropine. The percentage has increased sharply for some compounds, e.g. phenacetin which is now the most common adulterant, it has increased from a minor adulterant 1.6 % to a large value of 40.6 % of samples. The Brunt study gave valuable information about the diverse effects of impure cocaine samples, but there are no clear explanations for these effects. It recommended conducting further studies to give a full explanation and connect the route of administration with those effects. In many cases there is no information about some pharmacologically active compounds when they are administered nasally or other routes similar to those used in cocaine administration. Also, the drug users did not report the dose which caused adverse effects and whether there is a combination with other drugs or alcohol [19].

In 2010, Evrard et al. reported the composition and purity in street samples of cocaine [18]. Moreover, they aimed to study the effects of diluents in combination

with cocaine as occur in street samples on the health of users. This study recognised that the effects on users arise from the interaction between the cocaine and the diluents, not from each one alone, especially where impurities or diluents are pharmacologically active. Also, this study was the first to compare the results from forensic analysis with users' opinions about their cocaine samples. There was a huge difference between the analytical results and users' perception of purity and diluents and/or cutting agents. They found that users have incomplete knowledge about "cocaine" contents and gave some reasons to explain why they do not have enough information about their cocaine used, as they depend on dealer information, and they assess the quality depending on the price as we do with usual commodities. More studies should be conducted to study the effects of different modes of administration and cocaine content on the users [18].

Pagano and his co-authors in 2013 used NMR techniques for the investigation and identification of trafficking routes [49]. They designed and used ^1H NMR techniques and multivariate analysis to find the fingerprint of cocaine samples and study the link between samples [28] [49]. They aimed for a combination of the two methods in order to refer to distribution networks and the origin of the seized samples in Italy from different places and at different times. The outcome of this approach may be of help to the police in their investigation strategies [49].

Henderson and his co-authors [50] tried to accomplish a complete identification of unknown structures to characterize forensic samples. Their analysis was based on one and two dimensional NMR techniques to identify the samples which contained the toxic natural product, scopolamine. The confirmation of NMR results was carried out by using electrospray ionization ion trap mass spectrometry (ESI-MS) [50]. El-Gindy and his co-authors [51] mentioned, in their review, the application of infrared (IR) spectroscopy in chemometric studies. Chemometrics is the combination of statistical and mathematical methods with analytical data that allows the analysis of a huge collection of data to extract useful information. FT-IR alone or in combination with other analytical techniques can provide a collection of data for statistical methods to determine the required information [51, 52]. Rodrigues and his co-authors [52] reported the application of FT-IR to build a principal component analysis (PCA) model for 91 samples of cocaine. They used gas chromatography-mass spectrometry (GC-MS) to detect the adulterants and to identify cocaine for seized samples in Brazil. They found out that the purer samples were discriminated in one principal component

while other samples that include two forms of cocaine and other adulterants were discriminated in a different principal component [52].

The concept of comparative analysis is to carry out a comprehensive test of physical and chemical characteristics of drug samples to agree about the level of origin compared with other samples or groups of samples [53]. Besacier [54] developed a methodology used for the comparative chemical analyses of illicit drug seizures. The procedure consisted of three steps which aimed to standardise the method of analysis of the drug samples to allow rigorous sample/sample comparisons (tactical intelligence) and, with the use of authentic compounds, to obtain information on geographical and/or synthetic route. The first step is the identification and quantitation of major and minor components. It may include opium alkaloids and derivatives in the case of heroin samples, and diluents and adulterants. The second step is the characterisation of manufacturing impurities and by-products in illicit drugs. This step generates the drug signature which is characteristic of origin. The third step is isotopic analysis of the drug sample. There are many parameters that could modify the isotope contents e.g. environment (humidity, temperature), photoperiod, and its constituents. They used GC-FID in the first two steps of this procedure and gas chromatography-isotope ratio mass spectrometry (GC-IRMS) in the third step. They then applied principal component analysis (PCA) in their data analysis. They concluded that the first step is the basis of the procedure, while performing steps 2 and 3 act as confirmatory methods [54].

The previous analytical techniques rely on the chemical structure and chemical properties of the materials and either the chromatographic or spectroscopic techniques to profile the samples and to identify and quantify the drug and the adulterants. One technique that is based on the physical properties of the samples, allowing a study of their purity and thermal behaviour, is Differential Scanning Calorimetry (DSC) [55, 56]. DSC can be used to study changes in crystal forms, melting points and thermal degradation behaviour of authentic materials as well as impure samples [56]. Medeiros and his co-authors [55] developed a method to identify the components of Merla (or Mela, that is the residual sediment with its low cocaine concentration) due to the difficulties of identification of organic and inorganic components in the same samples by other chromatographic techniques, e.g. HPLC, or difficulties in quantification of the components by TLC. They used thermal analysis techniques DSC and thermal gravimetric (TG) analysis to obtain results about the Merla

composition, while they developed a chromatographic method by using GC to measure the relative amount of cocaine in the samples [55].

Cocaine is available in two chemical forms: as salt and free-base. The salt form is usually administered by snorting the crystal powder nasally or injecting an aqueous solution intravenously. The free-base form of cocaine is smoked using various types of available devices or pipes. Cocaine free-base melts at 89 °C, while (essentially at this m.p.) it is volatile above 90 °C; cocaine HCl melts at 195 °C [56]. However, the recovery of cocaine varies depending on the experimental conditions and applied temperature, as well as the form of the drug [56]. Smoking of the free-base cocaine in a tobacco cigarette was reported to give a percentage of recovery of cocaine of only 6 % only due the effects of other components of the tobacco leaves that reduce the recovery of cocaine [56]. In comparison, Perez Reyes et al. [57] heated the free-base at 265 °C in a glass pipe simulating smoking conditions, then they recovered 44 % of cocaine [57, 58]. Moreover, Novak and Saleminik have studied heating cocaine at a high temperature of 600 °C under nitrogen gas, and designed a model to study the degradation of cocaine; they identified 15 compounds [57-59]. Although the problems associated with smoking cocaine are more than the problems associated with snorting, and injecting cocaine, users keep smoking cocaine as it gives very rapid high and is more addictive than administering cocaine by other routes [60].

Martin and his co-authors [61] have studied the percentage of the main products of pyrolysis of cocaine during volatilisation. They collected cocaine and the by-products in three traps (ethanol, acidic, and basic). They found that the percentage of benzoic acid and methyl ecgonidine increased sharply from 6 and 2 % to 83 and 89 % respectively when they raised the temperature from 260 to 650 °C. This increase in the pyrolytic products was associated with a decrease in the amount of intact cocaine from 60 % to 2 % only when they increased the temperature. Additionally, they studied the impact of flow rate on the amount of cocaine recovered. They concluded that the pharmacological impacts of smoked cocaine rely greatly on the conditions of volatilisation [61]. Gostic [56] and his co-authors studied the thermal decomposition at 450 °C of impure cocaine samples under aerobic pyrolysis conditions. They used GC-MS for identification of pyrolysis products and also to quantify some of them, the confirmation for the results was carried out by NMR spectroscopic techniques. DSC was used to obtain important results on melting points of pure authentic materials, impure samples, and the volatilisation behaviour of the analysed mixtures [56]. They

reported that they recovered available for inhalation approximately 76 % of cocaine in the traps, and the measured the pure adulterants (paracetamol, benzocaine, phenacetin, lidocaine, procaine, and caffeine) totally recovered under the same conditions. In the case of impure samples of cocaine, they found adulterants altered the thermal behaviour of cocaine compared with pure samples [56].

The associated harms with smoking crack cocaine are the problems caused by the pyrolytic products of cocaine e.g. methyl ecgonidine which is produced by smoking cocaine and was used as a biomarker in the biological fluids of crack smokers [16]. Scheidweiler and his co-authors [16] studied the pharmacodynamics and pharmacokinetics of methyl ecgonidine and ecgonine by administering them to sheep. They recorded hypotension and tachycardia in all three sheep in their study [16].

This is the first attempt to use profiling results of crack samples to design an educational harm reduction message for crack smokers. This study will provide laboratory results to inform the crack users about the content of street seized samples and the differences between crack smoking tools. The educational message aims to increase the knowledge and awareness towards the associated harms and risks with users smoking behaviours. It could help to reduce those harmful consequences and encourage crack users to use less harmful equipment and be engaged in drug services because there is no treatment or service available for crack smokers currently compared with other drug users e.g. needle programs, substitution therapy.

Chapter 3

Experimental

3.1. Materials

Cocaine hydrochloride was purchased from Ferris & Co., Bristol, UK. Phenacetin, D-(+)-glucose, procaine HCl, and sucrose were purchased from BDH Chemicals, UK. Benzocaine B.P. was purchased from J. M. Loveridge, UK. Eicosane, levamisole, lidocaine, potassium bromide, acetonitrile, diethylamine, triethylamine, methanol, deuterium oxide, deuteriated dimethyl sulfoxide (d_6 -DMSO), deuteriated methanol, and deuteriated chloroform were purchased from Sigma-Aldrich, UK. Crack cocaine samples were provided by the Police in Swindon, UK.

3.1.1. Cocaine free-base preparation

Cocaine HCl was weighed accurately (1.0005 g), then the glassware was washed with water (3 x 25 mL) then with dichloromethane (DCM) (3 x 20 mL) to prevent any possible contamination. 1 g of cocaine HCl was dissolved in water. The free-base of cocaine was precipitated by adding ammonia until a basic pH was reached. Cocaine free-base was extracted three times with DCM (25 mL). The DCM extracts were collected in a conical flask. The ammonia layer was collected in a conical flask. The DCM solution was transferred to a separating funnel, and then washed with water (3 x 25 mL) to remove any residual of ammonia or ammonia chloride from cocaine base. If an emulsion formed, then water (1-2 mL) could be added to break the emulsion without shaking, just waiting. The DCM layers were collected in a clean conical flask and dried (Na_2SO_4 , 5-10 g), filtered and evaporated to dryness in vacuum ($\sim 40^\circ\text{C}$, rotatory evaporator). The flask with the sample was weighed = 38.1964 g; sample weight = 0.7263 g, yield 81 %.

3.1.2. Description of seized crack samples

The seized samples were provided from the Police in Swindon, UK. The samples were seized at different times between 2005 and 2008. They were supplied in many batches, each one contained varying number of bags and foils containing powder, rocks, or both. Also the weight of the samples varied between a few

milligrams and a few grams; this was a reason to optimise two protocols for the analysis. One of the batches had a barcode (B 4482929, DRS 8616, MES/01). The sample was given another code also (F263408), it contained 39 subsamples. They were named 1a-1z, 1aa-1mm, they were seized in 2008. Ten out of 39 samples were chosen randomly for the profiling, their weight ranged between 133-312 mg with sample codes: F263408 (1a, 1f, 1l, 1k, 1s, 1w, 1y, 1bb, 1kk, 1hh). The second batch supplied had various subsamples within plastic bags and foils. They were coded (B 4482929, DRS 8616, MES/02, F263408). Ten samples were chosen randomly, their weights ranged between 126-232 mg with sample codes: F263408 (2a, 2e, 2h, 2k, 2p, 2s, 2v, 2z, 2ee, 2gg). The third batch supplied had various subsamples within plastic bags and foils. They were coded (B 4482929, DRS 8616, MES/03, F263408). Another ten samples were chosen randomly, their weights ranged between 82-285 mg with sample codes: F263408 (3c, 3g, 3j, 3l, 3q, 3t, 3x, 3bb, 3jj, 3mm). The fourth batch supplied had various subsamples within plastic bags and foils. They were coded (B 4482929, DRS 8616, MES/04-10, F263408). This batch contain 15 subsamples, they were all analysed, sample codes: F263408(4a, 4b, 5a, 5b, 5c, 5d, 5e, 6a, 6b, 6c, 7a, 7b, 8, 9, 10).

Another batch was supplied from a group of samples seized in 2008. This contained 24 samples distributed into 8 bags. The barcode was (C 01609400, DRS 8698, F314608), samples (F314608/7.1-7.7) were separated in different bags, those samples weights ranged between 100-300mg, and other bag labelled the samples (F314608/7.8-7.24), this sample weight was ~5 g. The samples were off-white powders and lumps. Sample F314608/7.7 only contained a tiny amount.

A mixture of different samples were supplied, it contained nine samples, seized between 2005 and 2006. Their codes were: JGG01786A, JGG01786B, JF604140, 190340, JG6000323-1, JG6000323-2, F0867/08, 202506, D10377770, their weights ranged between 0.12 g and 2.9 g. They had different appearances, some had off-white or white colour, and the samples were powder, rocks, crystals, or a mixture of them.

Two crack samples (J00601197, J00601194) were ground and homogenised to use them as reference sample. This could be used to run repeated experiments to avoid the differences between unknown crack samples.

3.2. Experimental

Crack cocaine analysis protocol for HPLC, GC-FID and NMR analysis.

Two different protocols were used for routine analysis of crack cocaine samples. In each case the street sample of crack cocaine was weighed, powdered and thoroughly mixed.

3.2.1. Methods of profiling crack samples

Protocol (1) of crack cocaine analysis

1. 10-15 mg was taken, DCM (2 mL) was added and mixed by vortex (5 s). Vortex-2 genie (Scientific Industries, USA).
2. Deuterium oxide (2 mL) was added and mixed by vortex (5 s).
3. The mixture was centrifuged at 3000 rpm for 3 min.
4. DCM layer (1 mL) was diluted to 10 mL with methanol and then injected into HPLC; if necessary the solution was diluted further to bring the peaks on-scale.
5. Then, likewise, the D₂O layer (1 mL) was diluted to 10 mL with methanol and then injected into HPLC; if necessary the solution was diluted further to bring the peaks on-scale.
6. The rest of the DCM layer was used in HPTLC analysis.
7. A further 10 mg sample of the crack cocaine was dissolved in d₆-DMSO (dimethylsulfoxide) to carry out ¹H NMR analysis.

Protocol (2) of crack cocaine analysis

This protocol was suggested in the case the seized samples were not enough to run all the tests (all the steps of this protocol were not applied in this study).

Accurately weighed samples (up to 30 mg) were dissolved in DMSO-d₆ (2 mL) and analysed by NMR. The DMSO solution was diluted to 10 mL with methanol and then injected into HPLC.

Infra-red spectroscopy (FT-IR) was carried out on a Spectrum 65, FT-IR spectrometer (Perkin Elmer, USA). Crack samples (1-5 mg) were ground separately with anhydrous potassium chloride (~10 mg) and compressed at 10 tons to form a thin disk

which was scanned in the range 700-4000 cm^{-1} . Samples of authentic standards were prepared using the same method.

Mass Spectrometry (MS) with ElectroSpray Ionization (ESI) was carried out on a Bruker MicroTOF. Positive ion spectra were recorded.

Samples (1-2 mg) were provided in glass vials to the Department of Pharmacy and Pharmacology MS service for high-resolution (HR) ESI MS which yielded the $(\text{M}+\text{H})^+$ or $(\text{M}+\text{Na})^+$ mass ion and some fragmentation data.

Nuclear Magnetic Resonance (NMR) spectroscopy was carried out using a Bruker Avance (400 MHz) spectrometer.

The collected data were integrated and the chemical shifts of the peaks used to assign all the peaks for cocaine and any other cutting agents. These data were collected to use in the principal component analysis (PCA). The spectrum was calibrated and converted in numeric tables to export to the software for the PCA analysis.

Ultraviolet spectroscopy (UV) was carried out using a Lambda EZ201 UV/VIS spectrometer Perkin Elmer (USA).

A 0.1 % solution in methanol was prepared of cocaine and other standards. Each solution was scanned in the range 200-600 nm. Peaks of maximum absorption were determined to be used for detection in HPLC.

High Performance Thin Layer Chromatography (HPTLC) was carried out using a CAMAG (Switzerland) Horizontal Development Chamber.

HPTLC Plate: DC-Fertigplatten (Machery-Nagel, Germany); stationary phase: Silica Gel GF254

Mobile phase: Cyclohexane: toluene: diethylamine (45:45:10) (v/v/v)

Sample: (1-5 μL) Dichloromethane (DCM) layer of crack sample.

Standards: Cocaine HCl (1 mg/mL in methanol) 5 μL

Benzocaine (1 mg/mL in methanol) 5 μL

Phenacetin (1 mg/mL in methanol) 5 μL

The plate was pre-equilibrated for 20 min then developed to 7 cm.

Detection: UV at 254 nm, then sprayed with Dragendorff's reagent and observed in visible light.

Gas Chromatography/Flame Ionisation Detection (GC/FID) was carried out on a Chrompack CP2001 (Netherlands) CP2001 instrument. The DCM layer obtained using protocol A was diluted with ethyl acetate to 10 mL and injected onto the GC

capillary column. Temperature program: 180 °C for 5 min, then raised to 220 °C over 5 min (8 °C/min), then held at 220 °C for 10 min, detection with FID. The column was ZB (PEG) (10 x 2.5 mm, with 0.25 µm film depth). Mobile gas was He (Helium).

High Performance Liquid Chromatography (HPLC) was carried out with UV/vis detector Perkin Elmer (Shelton, USA).

Column: 150 x 4.60 mm, Gemini 5µ C18 110A (Phenomenex, UK) held at 35 °C.

Mobile phase: H₂O: acetonitrile: THF: triethylamine (580:360:60:0.5 v/v/v/v).

Detection: UV detector λ = 249 nm (0-4 min), 297 nm (4-9 min), 233 nm (9-11 min).

Sample: 1 mL DCM layer from sample preparation protocol A was diluted with methanol to 10 mL, and 20 µL was injected onto the column. The elution time was about 11 min; if the solution was too concentrated, the solution was further diluted with methanol 1 to 10 and re-injected. A similar protocol was carried out with the D₂O layer to analyze the components in the aqueous layer.

Standards: Cocaine HCl, benzocaine, and phenacetin standard solution in methanol were prepared in advance in order to generate the respective calibration curves.

3.2.2. Calibration curves by HPLC

Calibration curve of cocaine HCl

A standard solution of 1 mg/mL was prepared as stock solution in methanol, and diluted with methanol to serial concentrations of 0.05, 0.1, 0.2, 0.4, 0.6 mg/mL. Each was injected three times and the area under the curve (AUC) was measured.

Calibration curve of cocaine free-base

Cocaine free-base was prepared by conversion of cocaine hydrochloride using the procedure mentioned above. 1 mg/mL stock solution was prepared then other concentrations were prepared by dilution the stock one at 0.05, 0.1, 0.2, 0.4, 0.6 mg/mL. Each was injected three times in HPLC and the area under the curve (AUC) measured.

Calibration curve of phenacetin

Low concentrations calibration curve of phenacetin

A stock solution of phenacetin 1 mg/mL in methanol was prepared and diluted with methanol to give a series of solutions of 0.01, 0.02, 0.04, 0.06, and 0.1 mg/mL. Each was injected three times each one and the area under the curve (AUC) was measured.

High concentrations calibration curve of phenacetin

A stock solution of phenacetin 1 mg/mL in methanol was prepared and diluted with methanol to give a series of solutions of 0.01, 0.05, 0.1, 0.2, and 0.4 mg/mL. Each was injected three times and the area under the curve (AUC) was measured.

Benzocaine calibration curve

A stock solution of benzocaine 1 mg/mL in methanol was prepared and diluted with methanol to give a series of solutions of 0.01, 0.05, 0.1, and 0.2 mg/mL. Each was injected three times and the area under the curve (AUC) was measured.

Procaine calibration curve

A stock solution of procaine 1 mg/mL in methanol was prepared and diluted with methanol to give a series of solutions of 0.01, 0.05, 0.1, and 0.2 mg/mL. Each was injected three times and the area under the curve (AUC) was measured.

HPLC validation

Two analysed street samples containing cocaine free-base and phenacetin as the major components were combined (to give a sufficient total weight), powdered and thoroughly mixed to provide a reference sample of street crack for use in all the method validation procedures.

The mean content of cocaine and major cutting agents in the DCM layers was calculated and then the content in the D₂O layer was added to measure the total content in the samples.

3.2.3. Calibration curves by GC-FID

As in the preparation of the calibration curves in HPLC, standard solutions for cocaine and the common adulterants were prepared, but in the case of the GC-FID method, an internal standard (IS) was added to the solution because the injected amount of the solution is not reproducible quantitatively. Eicosane (C₂₀H₄₂) was

chosen as the IS, after experiments to show it exhibited base-line resolution from the cocaine and any impurities. A stock solution (1 mg/mL) in ethyl acetate was prepared. A mixed stock solution of cocaine free-base, phenacetin, and benzocaine (1 mg/mL) in methanol was prepared. The final solutions contained: 0.02, 0.05, 0.1, 0.2, 0.3, 0.4 mg/mL of cocaine free-base, phenacetin, and benzocaine and a fixed concentration of IS (0.15 mg/mL). Each solution was injected 3 times. The AUC of each analyte (cocaine, phenacetin, benzocaine, and IS) was measured and then the ratio of each AUC component to the AUC of the IS was calculated to draw the calibration curve.

3.2.4. Multivariate statistical analysis

Protocol A (separation content, CDCl_3 content analysis)

Crack samples were ground to a powder and homogenized. The sample was dissolved in two solvents system (CDCl_3 and D_2O). These solvents can dissolve polar and non-polar components. Samples from each of those solvents were used to run the NMR analysis.

Protocol B: whole content of samples (about 10 mg) was dissolved in 0.5 mL d_6 -DMSO and analysed.

NMR spectroscopic data were normalised according to the solvent peak (d_6 -DMSO) at 2.5 ppm. Then the peaks of the solvents (d_6 -DMSO, and D_2O) were deleted at ranges of (2.54-2.46 ppm, 3.58-3.34 ppm) to avoid any interference with sample peaks and the spectra were converted into numeric data to apply the statistical analysis. The spectra were chopped into intervals with 0.04 ppm width. The total spectra (1-10 ppm) were divided into 250 parts.

PCA was carried out using AMIX software, also SPSS was used for some analysis and graph plotting.

3.2.5. Differential Scanning Calorimetry (DSC)

DSC (DSC 2920 TA instrument, 30 L/min N_2 , 10 $^\circ\text{C}/\text{min}$, 50-275 $^\circ\text{C}$). DSC was used to run different samples and compare the impact of adulterants and crack samples.

Samples were divided into four groups:

1. Pure cocaine (HCl salt, and also free-base), authentic adulterants.
2. Mixtures of cocaine and other authentic adulterants in the same ratio as crack samples.

3. Series of three mixtures were prepared by physical mixing of cocaine and phenacetin. The concentration of cocaine decreased from 100 % in mixture 1 to 0 % in mixture 5.

4. Street crack samples.

Each sample was weighed precisely and run three times. Mixtures of cocaine and other adulterants were prepared in the same ratio of street crack samples.

3.2.6. Crack cocaine pipe smoking model

The choices made in the design of this model were decided after a meeting with a harm reduction worker who provided crack smokers with services through a drug project in Swindon. We acknowledge his help in this design. An experimental set-up (Fig 3.1) to mimic the process of crack smoking was devised. This comprised: a pump (GE G626X, USA) set to deliver an air flow rate of 30 L/min; three cold traps (cold fingers, -25 °C) in series containing glass beads (8 mm) to increase the surface area of deposition. An ACI (Andersen Cascade Impactor) with two stages to collect particles of 4.7 µ and 1.1 µ respectively; a connection to a customised mouthpiece. For preliminary experiments the mouthpiece was customised to a standardised crack pipe of a type known as a “Canadian Shooter” (Fig 3.2.c).

The shooter and brillo were weighed empty and then the sample was loaded onto the brillo in the shooter. The sample was melted slightly using a common cigarette lighter. The shooter including brillo and the sample were re-weighed, when the sample had solidified again to determine the actual sample weight in the run. After loading, the pipe was carefully heated with a micro-Bunsen burner and the temperature monitored by a temperature probe (TENMA 72-2065, OHIO). An air flow of 30 L/min was established through the pipe and maintained for 10 mins, this flow rate was chosen to mimic the smoking behaviour of crack smokers when they have a fast and deep breath as forced inhalation. After 10 mins, the airflow was stopped and compounds recovered from the pipe, traps and internal surfaces of the apparatus by dissolution in methanol separately. These solutions were analysed by HPLC (column: 150x 4.60 mm, Gemini 5µ C18 110A maintained at 35 °C. Mobile phase: H₂O:Acetonitrile:THF:triethylamine (580:360:60:0.5 v/v/v/v). Detection: UV/Vis λ= 249 nm (0-4 min), 297 nm (4-9 min), 233 nm (9-11 min). The cocaine

and phenacetin were measured separately to quantify the emitted dose and the amount that was left in the device.

The method was optimised using pure cocaine free-base and then a sample (reference crack sample) of street crack cocaine containing phenacetin as its main adulterant was examined using the same procedure. Three replicates over which the measured temperature fell within the range 90-130 °C were carried out. The metal piece “Brillo” was weighed after being washed and dried to determine whether any loss of weight occurred.

The efficiency of crack pipes will be studied using various available devices in the Department of Pharmacy and Pharmacology. However, there are many parameters that should be discussed with a HR worker, especially the temperature and the time of collecting samples. This discussion will provide us with more information about the habits and the conditions that users apply when smoking crack such as pipes, or other tools, the condition of smoking, crack sample preparation procedures. This kind of information is not available in published papers where most studies have their own design to get the results of their research question more than studying the same tools and pipes that are actually used by crack smokers. The aim of the model is to mimic the smoking process in humans and to trap any inhaled components of the crack cocaine either as particles (in the impingers) or as vapour. This trap followed two stage impingers using an Andersen Cascade Impactor (ACI) to separate the particulate material produced in the smoking process. Three cold traps, filled with glass beads to increase significantly the surface area and immersed in solid CO₂ in acetone, were used to collect the volatilized compounds. The traps were connected to a pump which controlled the flow rate of air through the model (Fig. 3.1).

The samples were loaded into one of three kinds of pipe (used in the street). The first is a typical soft drink metal can which is punched with a few holes and cigarette ash used on the holes to carry the melted crack sample. The second is a medical inhaler of the type used by asthmatic patients, but the crack abusers use it (in the reverse direction) simply as a conveniently shaped piece of plastic. The third is the Canadian shooter pipe which is a glass stem with a metal “Brillo” inside. Brillo is a piece of steel wool used to upload the crack sample on (Fig. 3.2). The mouth piece that connects each pipe to the smoking model was modified to accept the different pipes by using a rubber piece to hold the pipe connected to the model.

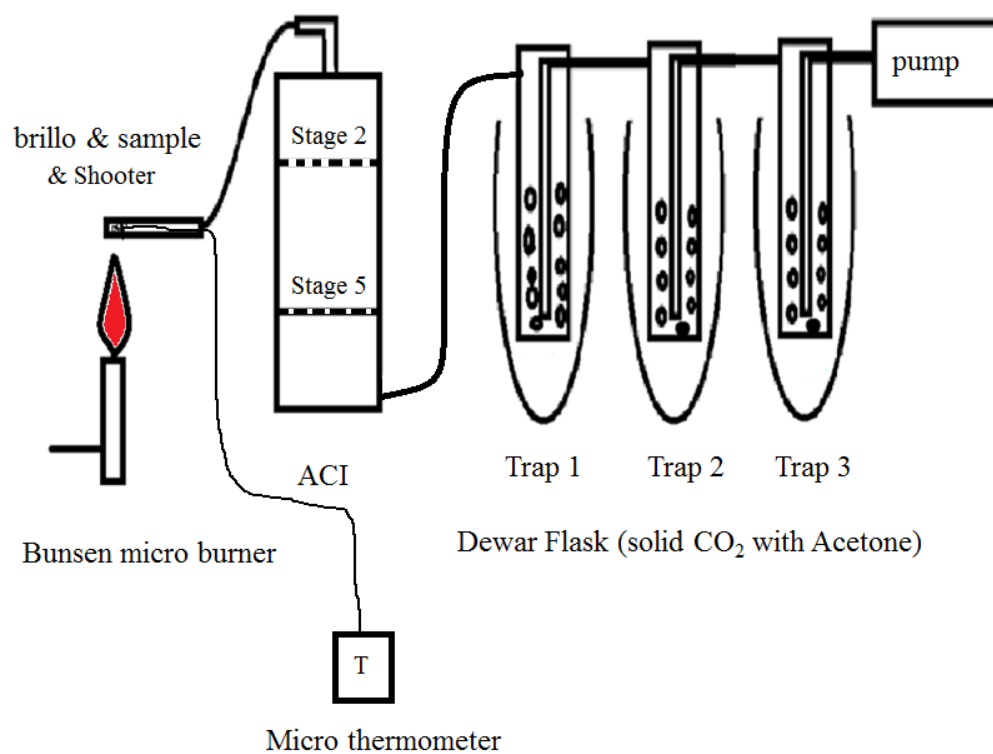


Fig 3.1. Crack smoking model.



Fig 3.2. Crack smoking tested tools: a. drink can, b. asthma inhaler, c. standardised shooter (“Canadian shooter”).

Chapter 4

Results and Discussion of Profiling Street Crack Samples

4.1. Introduction about profiling

The profiling process for a substance such as an illicit drug includes two interdependent procedures. The first one is to develop analytical methods that can provide a signature of the seized street drug samples. The second procedure is to use the results of analysis for intelligence purposes [34]. The changes in the drug market and the massive increase of demand have led to the production of more complicated products including the use of various cutting agents or production of synthetic drugs in clandestine laboratories. Characterization and impurities profiling has increasingly been used to supplement routine testing procedures. In addition, profiling tests can be used to differentiate between illicitly prepared drugs and those produced legally [62].

Profiling samples of illicit drugs aim to collect more information by applying varied analytical techniques to identify and quantify the components of the samples. The analysing of samples with essentially unknown content such as street-seized crack cocaine requires the use of more than one technique. It is necessary to identify and confirm each component then to quantify them by validated methods which may be different for the different components of a mixture.

4.2. Qualitative analysis

There are different levels of information that could be collected from qualitative techniques that are used in profiling studies. These techniques include thin layer chromatography (TLC), high performance thin layer chromatography (HPTLC), infrared spectroscopy (FT-IR), nuclear magnetic resonance (NMR) spectroscopy, and mass spectrometry (MS). They have different applications and yield different types of identification about a sample. Applying more than one of those techniques will provide more information than could be collected from only one method and may help to validate the results collected previously using other techniques. No single analytical technique can provide a full signature of unknown seized-drug samples.

4.2.1. High Performance Thin Layer Chromatography (HPTLC)

This is a rapid, economic technique that requires only a small amount of the sample. 20 x 10 cm plates were used in this study to enable the comparison of more samples under the same conditions [63]. Moreover, HPTLC can be used to quantify approximately the content if extra steps of extraction and injecting the extract into more quantitative techniques, e.g. HPLC, GC, are employed. However, with the available detection method of UV absorbance or chemical derivatization to produce coloured products, it is unlikely that all the components of a mixture will be detected. Unknown components cannot be identified without standards which must be applied to each plate in order to control variability in developing solvent composition.

Figs. 4.1 and 4.2 illustrate some representative HPTLC plates that provide a preliminary indication of the content and of the quantities depending on the intensity of the spots of each component compared with the pure standards applied at known concentrations. The lines within each column are representative of the components of each sample. This resembles a bar-code which can be similar for the same or for very similar samples. This analogy is potentially useful in conveying the idea of purity versus contamination to the HR target group of crack cocaine users. This gives an idea about the complexity in the content of the samples and how many compounds, e.g. drug, natural by-products, cutting agents, those samples include. The visual comparison between different plates can give an idea about the differences between different groups of samples and between batches of samples. This is a primary indication of the similarity of content in samples which may have the same source; this indication could help in tracking sources and channels of distribution of the seized crack cocaine.

It is clear from Fig. 4.1 that crack sample components look like a bar-code which is exclusive for each component as fingerprint. In this HPTLC plate, two crack samples were used. Sample 4 contains cocaine and phenacetin mainly, and other impurities which appeared in the concentrated sample. Sample 5 contains benzocaine as a major component and cocaine as a minor component.

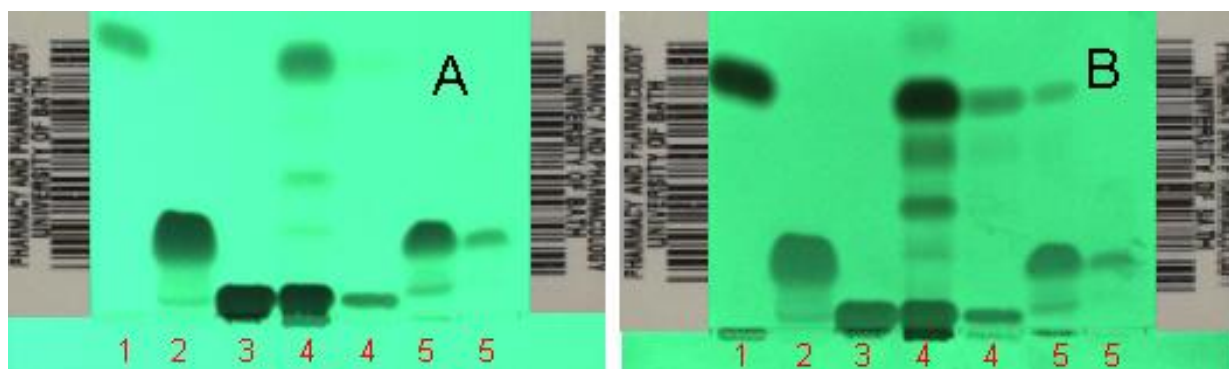


Fig. 4.1. HPTLC plate at 254 nm for crack sample J00601197 (4), 2931657A (5); 1 cocaine, 2 benzocaine, 3 phenacetin, 4 crack J00601197, 5 crack 2931657A. Visualisation: UV = 254 nm (A) and UV = 254 nm after spraying with Dragendorff's reagent (B).

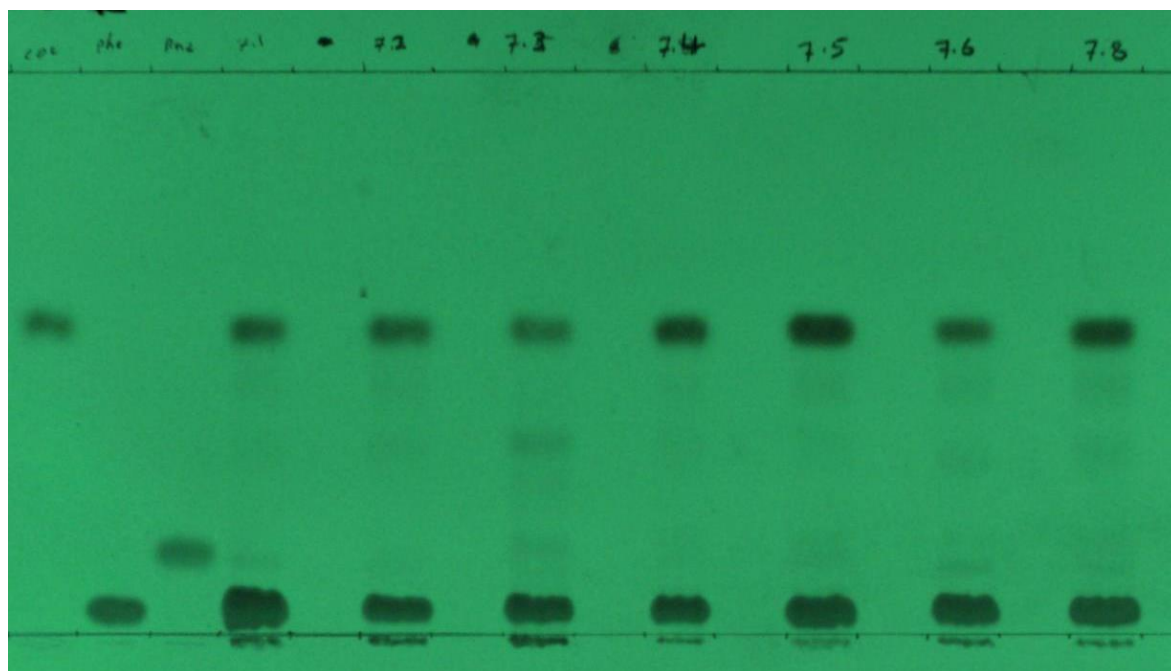


Fig. 4.2.a. Samples from the left: cocaine, phenacetin, benzocaine, crack samples (C 01609400, DRS 8698, F314608) 7.1, 7.2, 7.3, 7.4, 7.5, 7.6, 7.7 and 7.8. Visualisation: UV = 254 nm after spraying with Dragendorff's reagent.

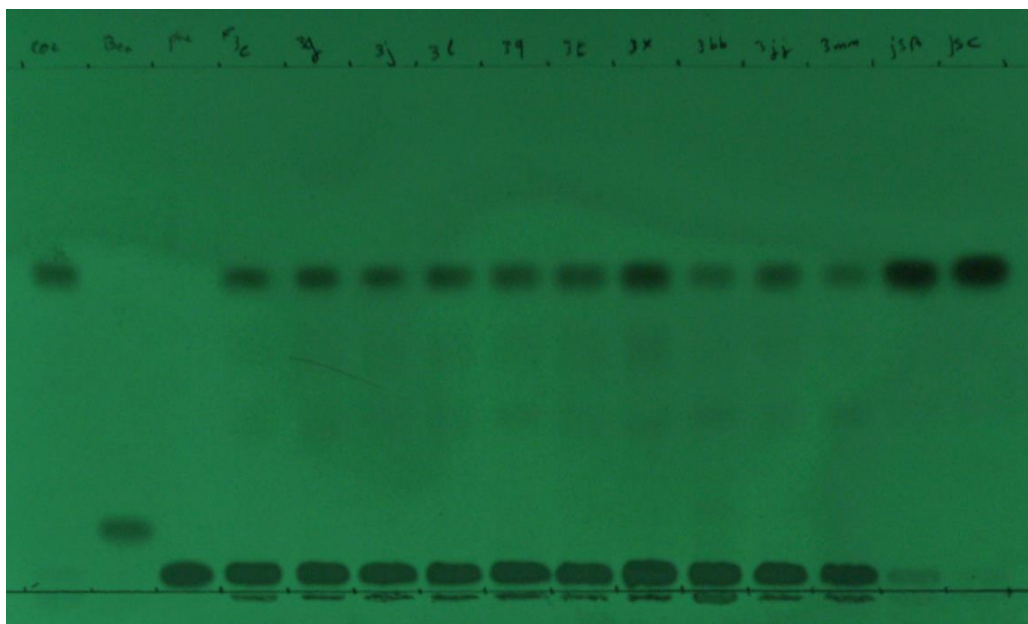


Fig. 4.2.b. Samples from the left: cocaine, benzocaine, phenacetin, crack samples (B 4482929, DRS 8616, MES/03, F263408) 3c, 3g, 3j, 3l, 3q, 3t, 3x, 3bb, 3jj, 3mm, and two pure crack samples JSA and JSC (100811). Visualisation: UV = 254 nm after spraying with Dragendorff's reagent.

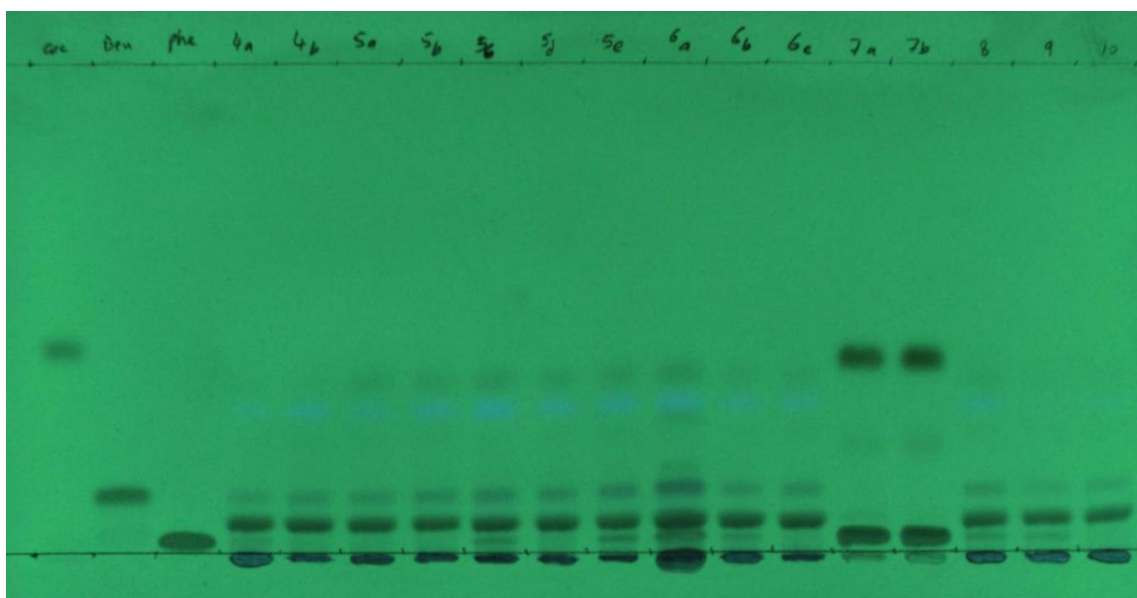


Fig. 4.2.c. Samples from the left: cocaine, benzocaine, phenacetin, crack samples (B 4482929, DRS 8616, MES/04-10, F263408) 4a, 4b, 5a, 5b, 5c, 5d, 5e, 6a, 6b, 7a, 7b, 8, 9 and 10 (110811). Visualisation: UV = 254 nm after spraying with Dragendorff's reagent.

Fig. 4.2. HPTLC for different seized crack batches.

Comparing the three groups of samples (Fig. 4.2.a, b, c) may represent the various cases of diversity of the content of samples in street. Fig. 4.2.a may represent the ideal case of similar samples (C 01609400, DRS 8698, F314608) that may have the same components at the same concentrations. This could be explained that those samples came from one batch and were divided into smaller samplers for distributing in street. Similarly, Fig. 4.2.b contains also similar samples which look identical to each other. On the right side of Fig. 4.2.b, there are two samples (JSA, JSC) are pure free-base cocaine prepared by converting cocaine hydrochloride into base form that were prepared with two different methods. The chromatogram of those two pure samples showed the differences between them and other street impure samples. So all these differences between pure cocaine free-base and crack samples indicate to cutting agents or by-products of illicit preparation methods.

Samples in Fig. 4.2.c have a diversity of samples including some that contain cocaine. This is the case when faked samples are distributed in the street as crack. This may lead to harmful effects to users when they consume such samples that may contain hazardous contents instead of cocaine. The outcomes of HPTLC can give a direction for further analysis to confirm the content and then to quantify each component. In the case of unknown components, more standards should be used and further analysis is required to assign the structure of other compounds.

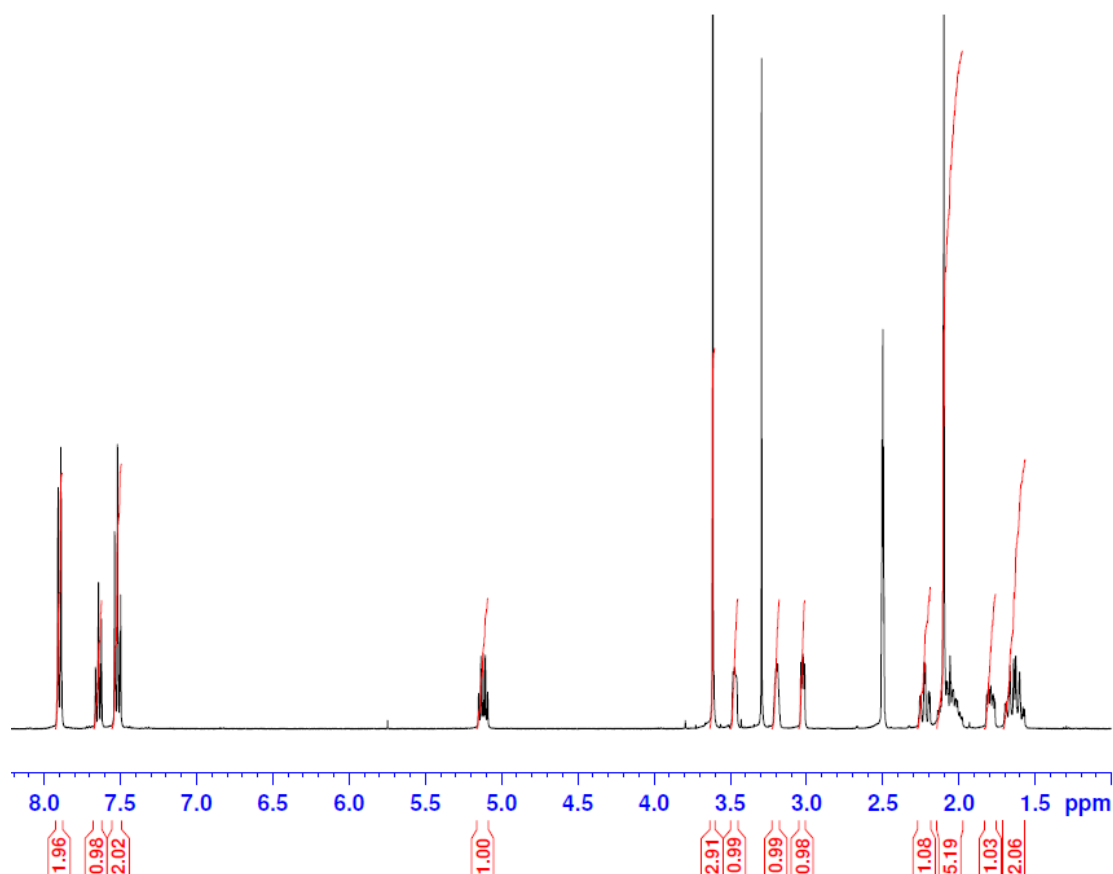
4.2.2. NMR spectroscopic analysis

Nuclear Magnetic Resonance (NMR) spectroscopy is widely applied in profiling procedures for many objectives. Proton NMR spectroscopy can determine the molar ratio of cocaine and adulterant compounds. It is also used widely in analytical chemistry to identify known and unknown organic compounds. Moreover, NMR spectroscopy can be used for semi-quantitative analysis by adding an internal standard or by evaluating the molecular ratio of the contents. In this study, NMR data were converted and used for principal component analysis (PCA) to track the distribution channel depending on the cutting agents that have been added at different levels of preparation and distribution [49, 64].

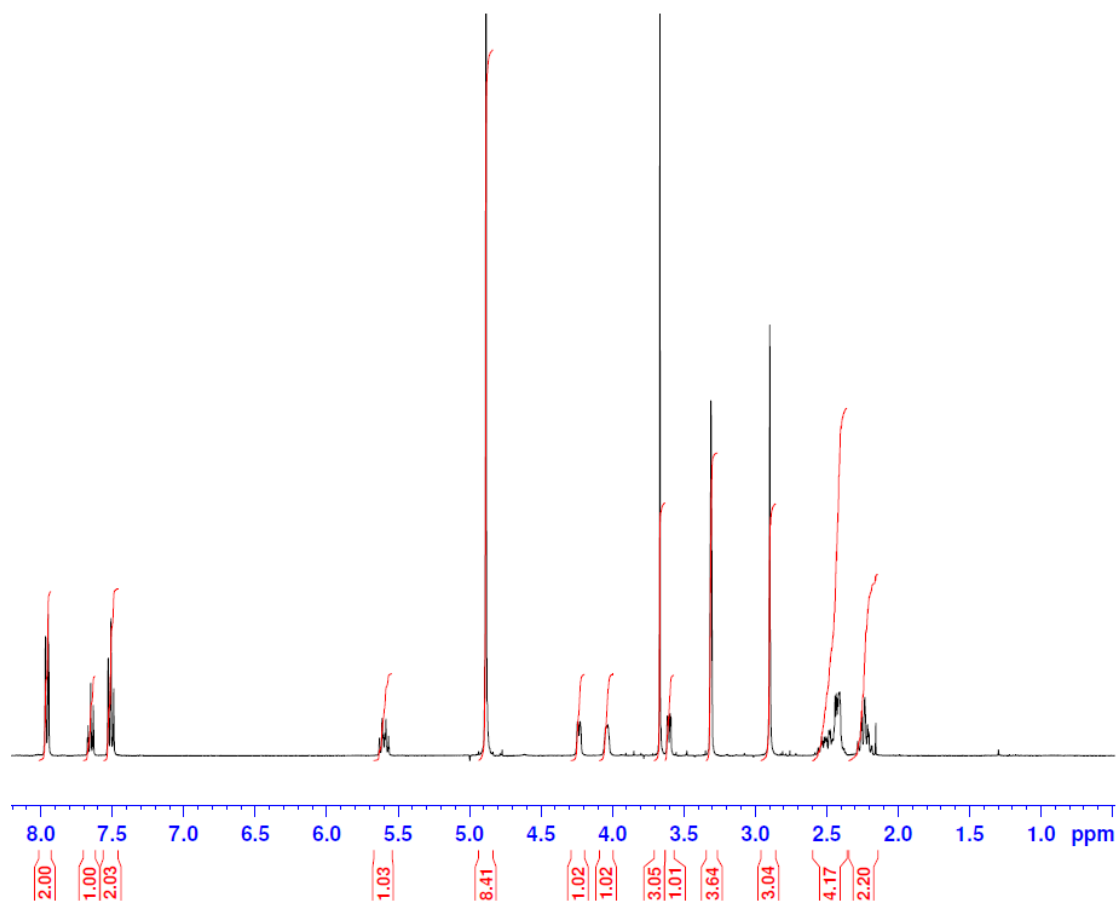
The main limitation encountered in using NMR spectroscopy in this study was to identify suitable solvents. In protocol A, CDCl_3 was used to dissolve non-polar

components and D₂O was used to dissolve polar components. This enabled the various cutting agents to be identified but over simplified the spectra for the PCA analysis. Thus, for PCA analysis, samples of seized crack were dissolved in d₆-DMSO which is suitable for both polar and non-polar compounds. NMR spectroscopy is a relatively insensitive technique and required about 20 mg of seized crack to detect the cutting agents or other minor components that are expected to be at low concentrations

Pure cocaine (Fig. 4.3) and pure standards (Fig. 4.5, 4.6, 4.7) were analysed to assign peaks in their spectra (Table 4.1, 3.2, 3.3), then crack street samples were analysed. It was clear how NMR spectra for crack cocaine samples could be used to identify the content of crack samples and the relative amount of each component depending on the peak intensities.



a. ¹H NMR spectrum of cocaine free-base (400 MHz, d₆-DMSO).



b. ^1H NMR spectrum of cocaine HCl (400 MHz, $\text{d}_4\text{-MeOH}$).

Fig. 4.3. ^1H NMR spectra of cocaine free-base and cocaine HCl.

Assignment of cocaine peaks was made as shown in the following table (Table 4.1) and are consistent with those reported for benzoylecgonine, a cocaine metabolite that lacks the methyl ester group [65].

Table 4.1

Cocaine free-base ^1H NMR data

| Chemical shift (δ) | Multiplicity | J (Hz) | Integral | Assignment |
|-----------------------------|--------------|--------|----------|------------------------------------|
| 1.63 | m | - | 2 (1+1) | $\text{CH}_2(6a), \text{CH}_2(7a)$ |
| 1.79 | m | - | 1 | $\text{CH}_2(4a)$ |
| 2.05 | m | - | 2 (1+1) | $\text{CH}_2(6b), \text{CH}_2(7b)$ |
| 2.09 | s | | 3 | $-\text{N}-\text{CH}_3$ |

| | | | | |
|------|-----|-----------|---|----------------------|
| 2.22 | d.t | 2.9, 11.5 | 1 | CH ₂ (4b) |
| 3.02 | d.d | 3.6, 5.2 | 1 | CH ₁ (2) |
| 3.2 | m | - | 1 | CH ₁ (5) |
| 3.47 | m | - | 1 | CH ₁ (1) |
| 3.61 | s | | 3 | -O-CH ₃ |
| 5.12 | m | - | 1 | CH ₁ (3) |
| 7.51 | t | 8.0 | 2 | (3', 5') |
| 7.64 | t.t | 1.2, 7.6 | 1 | (4') |
| 7.9 | m | - | 2 | (2', 6') |

2D NMR spectra of cocaine free-base (Fig. 4.4) showed correlations between protons up to three bonds apart, helping to confirm the assignment of the 1D spectrum and in some cases to assign the exact peak of similar protons in the spectrum.

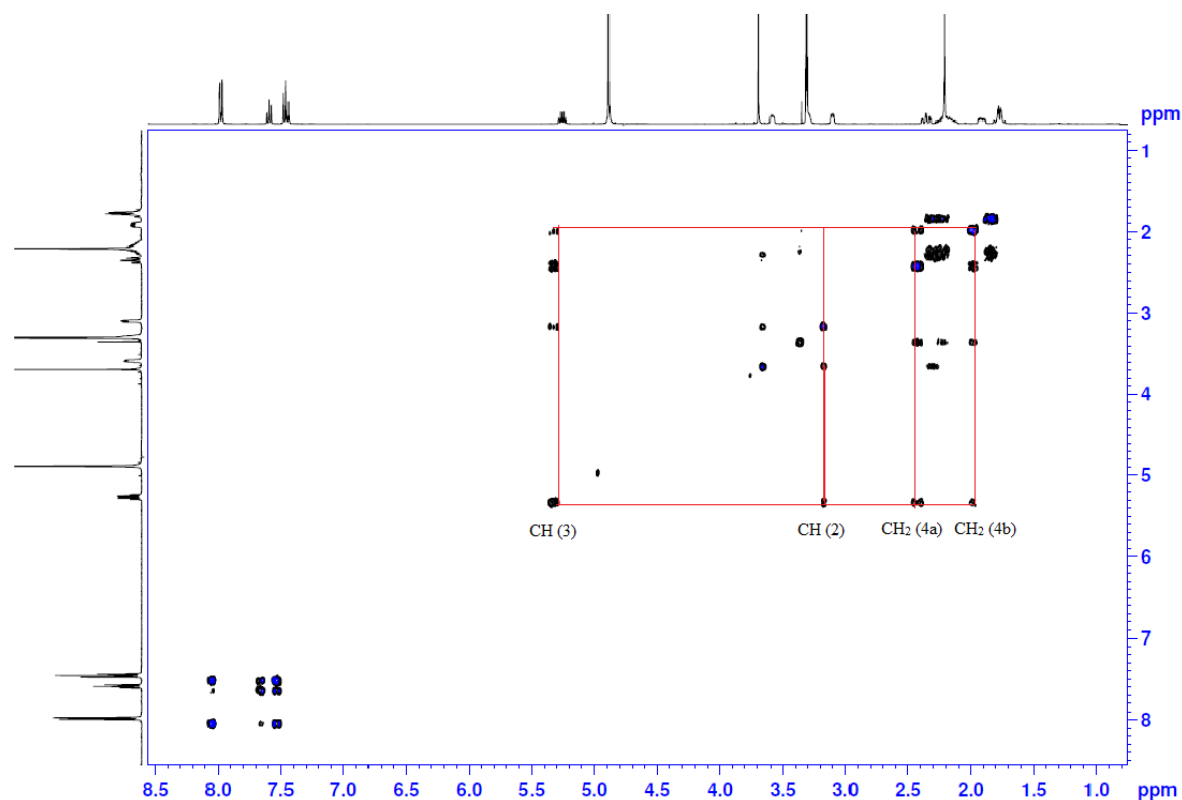


Fig. 4.4 2D NMR- COSY spectrum of cocaine base (d₄-MeOH).

Phenacetin is one of the most common adulterants used in crack cocaine samples. It has a simple structure compared with cocaine. It is identified in different countries as one of the main adulterants in cocaine samples although it does give rise to harmful effects.

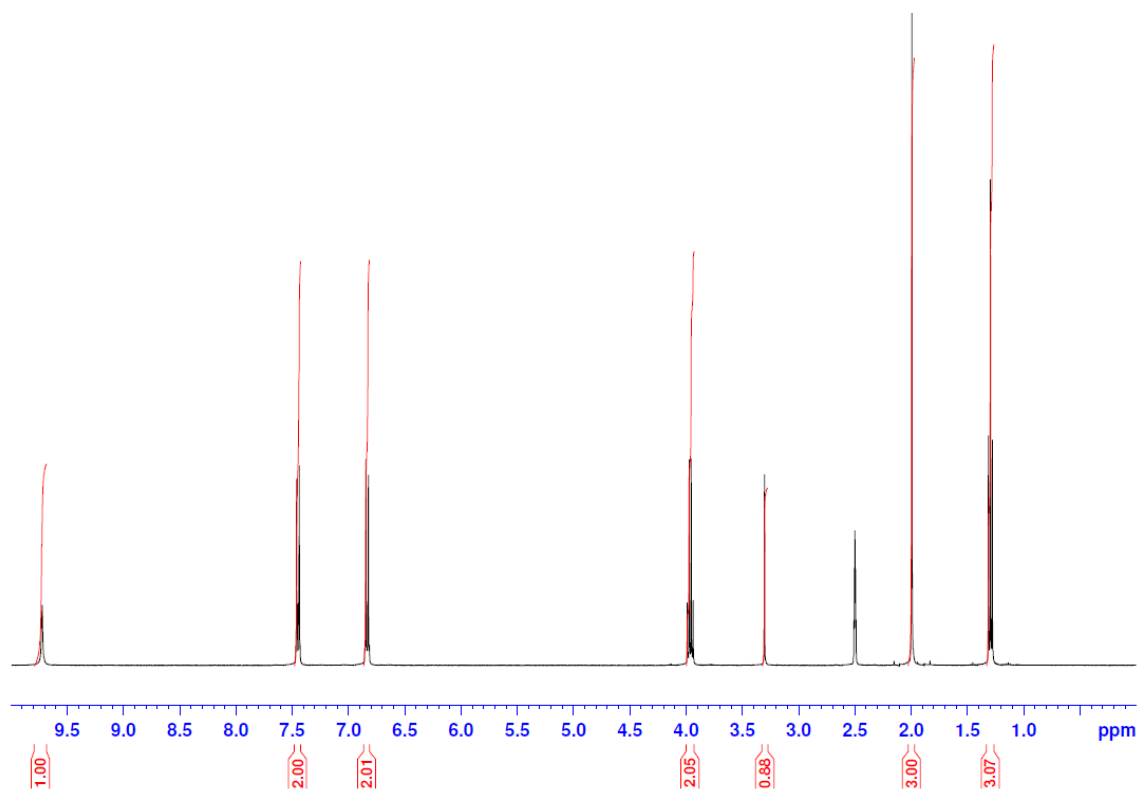


Fig. 4.5. NMR spectrum of phenacetin (400 MHz, d₆-DMSO).

The assignments of phenacetin peaks (Fig. 4.5) are in following table (Table 4.2).

Table 4.2

Phenacetin ¹H NMR data.

| Chemical shift (δ) | Multiplicity | J (Hz) | Integral | Assignment |
|--------------------|--------------|--------|----------|--|
| 1.35 | t | 7.0 | 3 | <u>CH</u> ₃ -CH ₂ - |
| 2.05 | s | | 3 | CH ₃ -C=O |
| 4.02 | q | 7.0 | 2 | CH ₃ - <u>CH</u> ₂ - |
| 6.89 | m | - | 2 | (2,3) |
| 7.5 | m | - | 2 | (1,4) |
| 9.78 | br s | | 1 | > N-H |

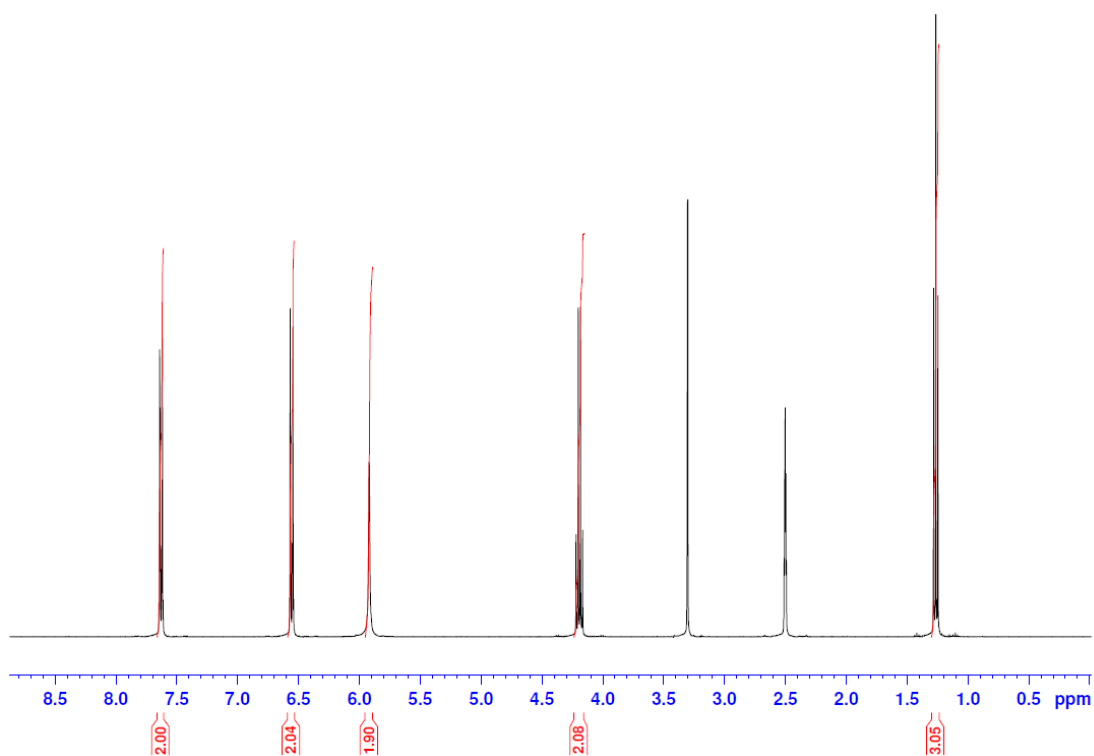


Fig. 4.6. ^1H NMR spectrum of benzocaine (400 MHz, DMSO).

The assignments of benzocaine peaks (Fig. 4.6) are in Table 4.3.

Table 4.3

Benzocaine ^1H NMR data.

| Chemical shift (δ) | Multiplicity | J (Hz) | Integral | Assignment |
|--------------------------------|--------------|--------|----------|-----------------------------------|
| 1.32 | t | 7.1 | 3 | $\text{CH}_3\text{-CH}_2\text{-}$ |
| 4.2 | q | 7.1 | 2 | $\text{CH}_3\text{-CH}_2\text{-}$ |
| 5.97 | s | - | 2 | -NH_2 |
| 6.6 | m | - | 2 | (2,3) |
| 7.6 | m | - | 2 | (1,4) |

Recently, levamisole a new cutting agent was identified in some countries, was used for human and animal treatment and it has increased in occurrence in the drug market during the last few years [66-68].

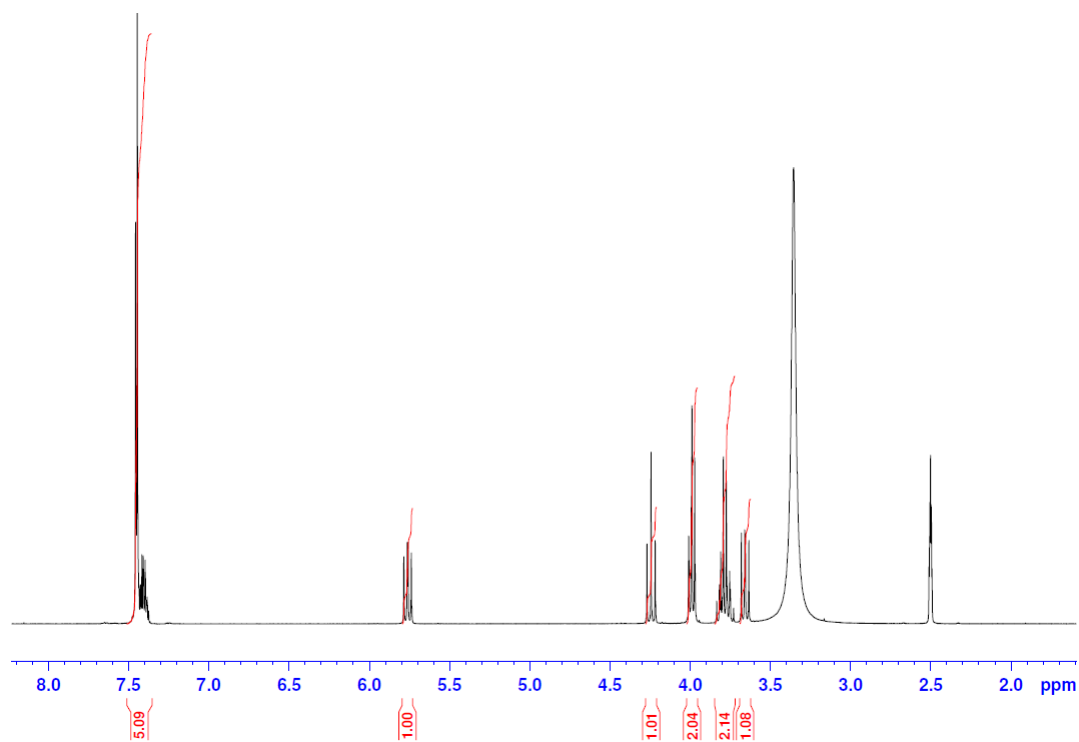


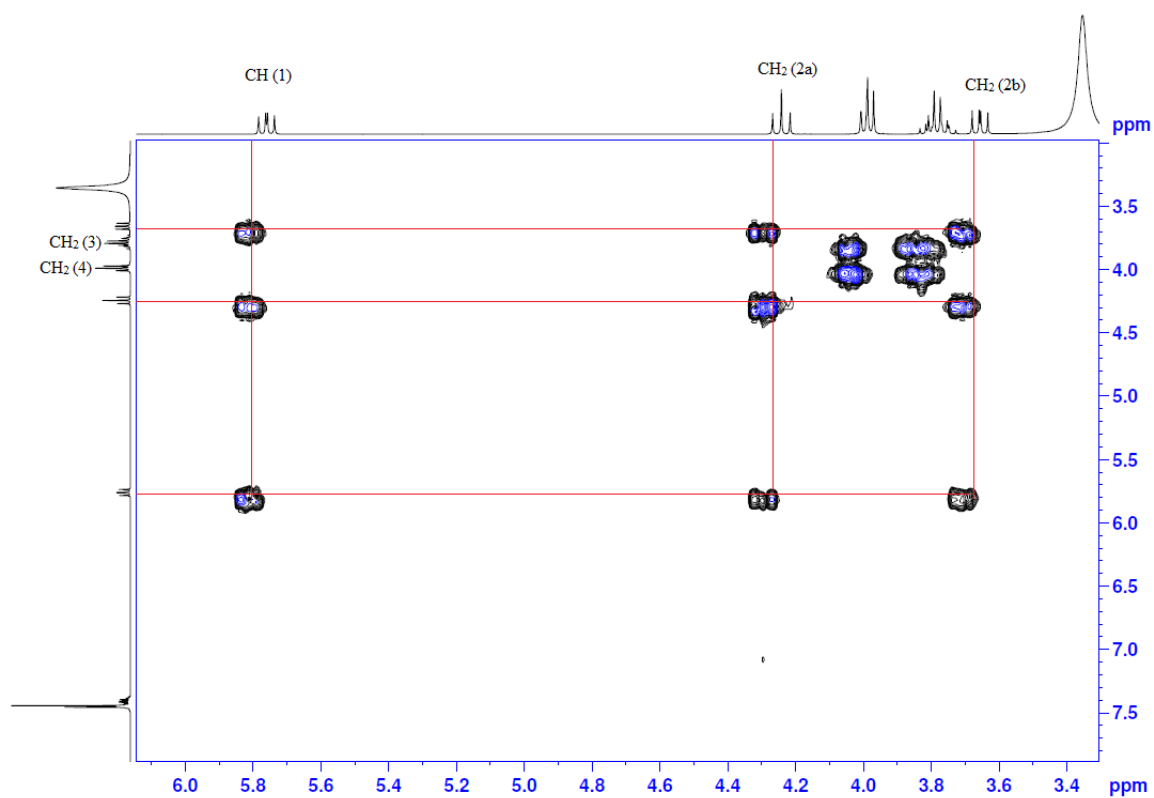
Fig. 4.7. ^1H NMR spectrum of levamisole (400 MHz, $\text{d}_6\text{-DMSO}$).

The assignments of levamisole peaks (Fig. 4.7) are in Table 4.4. 2D NMR analyses were used to assign the peaks.

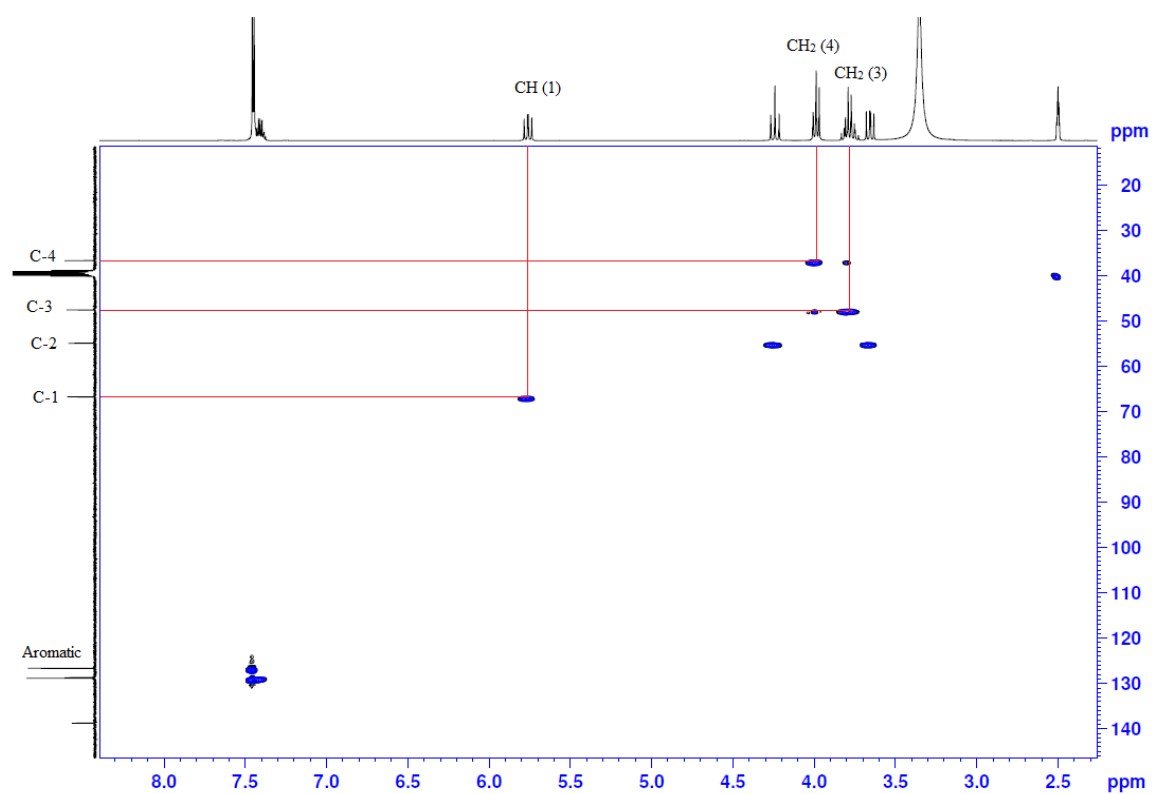
Table 4.4

Levamisole ^1H NMR data.

| Chemical shift (δ) | Multiplicity | J (Hz) | Integral | Assignment |
|-----------------------------|--------------|-----------|----------|--------------------|
| 3.65 | dd | 8.4, 10.4 | 1 | CH_2 (2a) |
| 3.8 | m | - | 2 | CH_2 (3) |
| 4.0 | m | - | 2 | CH_2 (4) |
| 4.25 | t | 10.4 | 1 | CH_2 (2b) |
| 5.75 | dd | 8.4, 10.4 | 1 | CH_1 (1) |
| 7.45 | m | - | 5 | Ar |



a. COSY spectrum of levamisole.



b. HSQC spectrum of levamisole.

Fig. 4.8 2D NMR spectrum of levamisole.

The HSQC spectrum (Fig. 4.8.b) that shows the correlation between the protons bound to the carbon next to the nitrogen atom at C3, and protons bound to the carbon (C4) next to the sulfur and confirms the non-equivalence of the proton at C2.

The samples analysed in this study did not contain levamisole. In general, the molar ratio of the main components may be determined by comparison of the integrals of distinctive peaks. ^1H NMR detects other components that are not visible either by HPLC or HPTLC, e.g. glucose, mannitol, and other water soluble diluents.

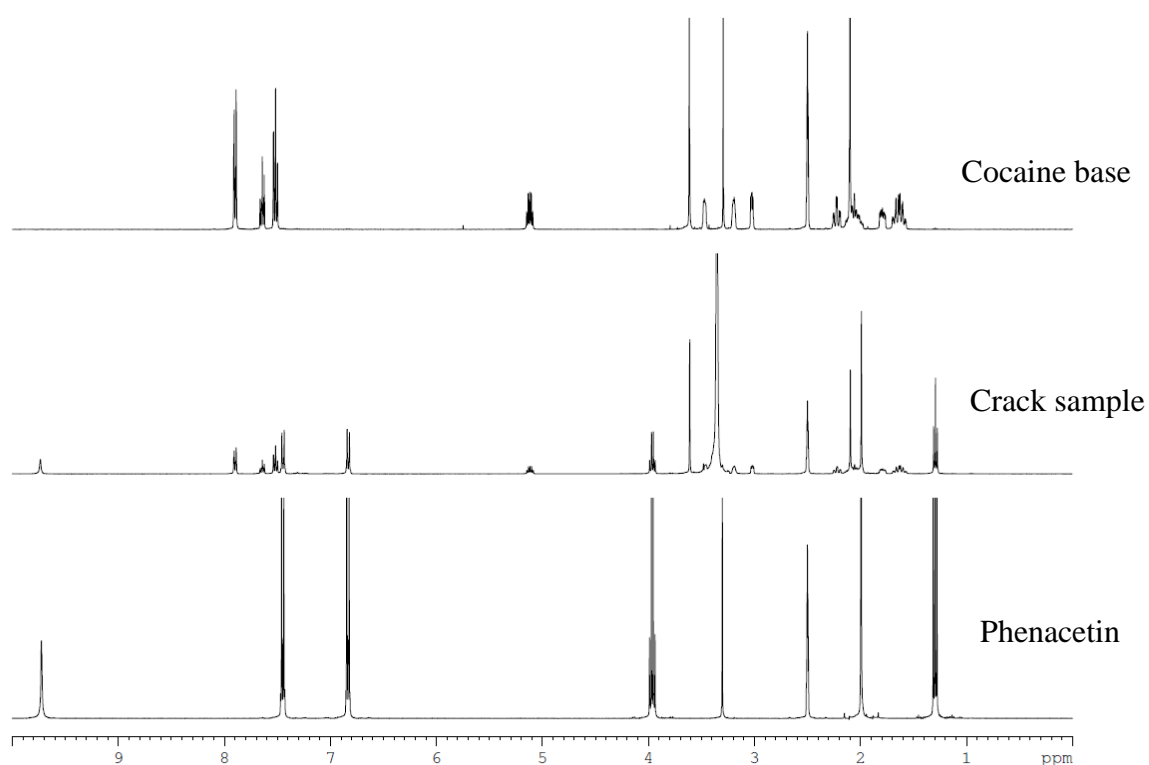


Fig. 4.9. ^1H NMR spectra (1) cocaine, (2) crack sample (REF), (3) phenacetin.

Fig. 4.9 shows the ^1H NMR of a crack sample and shows the main components cocaine and phenacetin by comparison with the standard spectra. The main peaks in the phenacetin spectrum resemble a bar-code that directly indicates that there is phenacetin in this sample. This bar-code could easily present the impurities in seized samples which could use later as a harm reduction message in an educational intervention. In the same way, the main peaks of cocaine form a cocaine bar-code which is helpful to distinguish among the samples and determine the components in the street crack samples. These samples are the same in Fig. 4.1 that confirm the content of crack sample compared with the pure authentic standards. In this way,

different analytical techniques confirm each other within the profiling procedures to confirm the content of analysed samples.

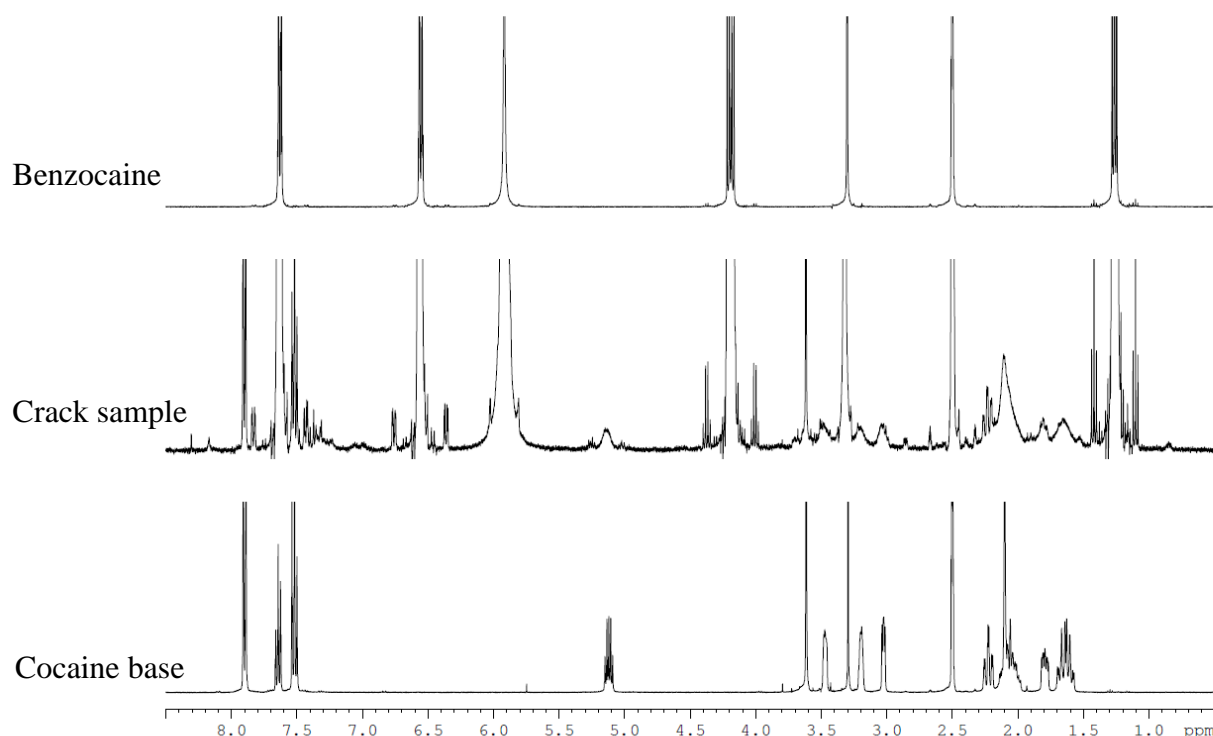


Fig. 4.10. ¹H NMR spectra (1) benzocaine, (2) crack 2931657C, (3) cocaine.

In Fig. 4.10, the crack cocaine sample contains cocaine together with benzocaine. This NMR spectrum shows that cocaine is a minor component of this mixture. The HPTLC results in Fig. 4.1 contained the same samples shown in Fig. 4.10 that confirm the content of the crack sample compared with authentic standards.

Crack sample JG 600323-2 contained cocaine free-base only without any cutting agents, e.g. phenacetin or benzocaine, compared with other crack samples provided by the Police from the same area. This could be evidence of more pure crack samples that cause higher health risks due to purity compared with other samples (Fig. 4.11).

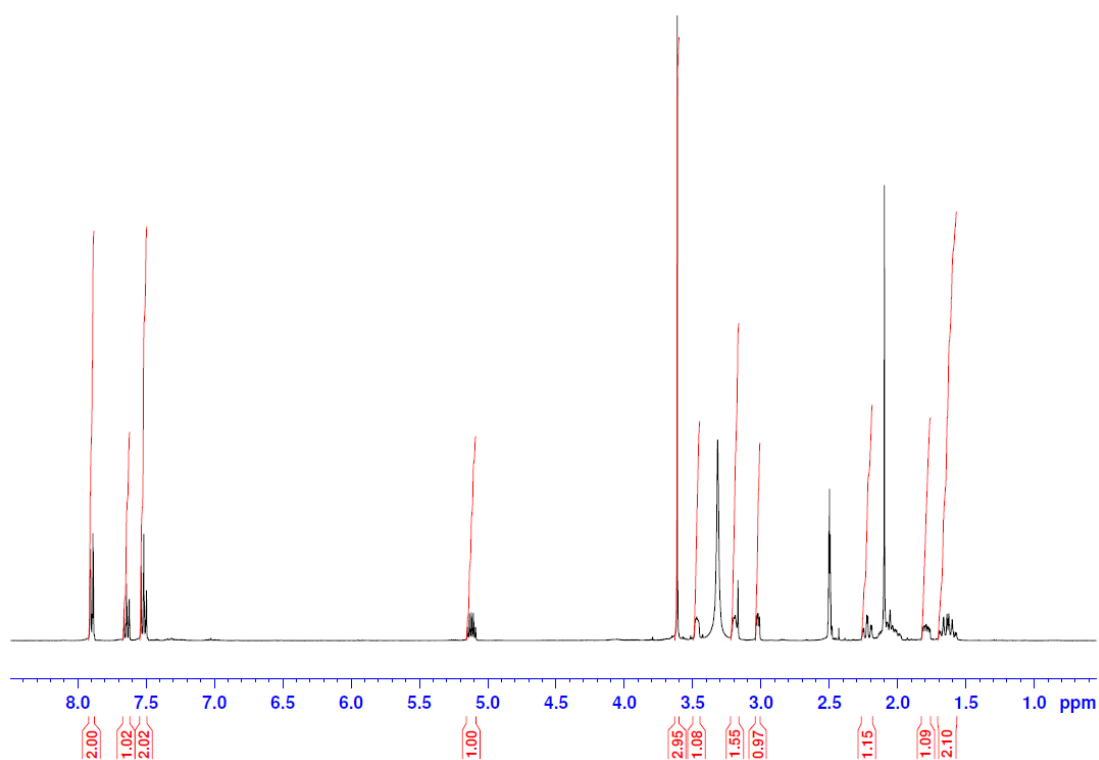


Fig. 4.11. ^1H NMR spectrum for crack sample JG 600323-2.

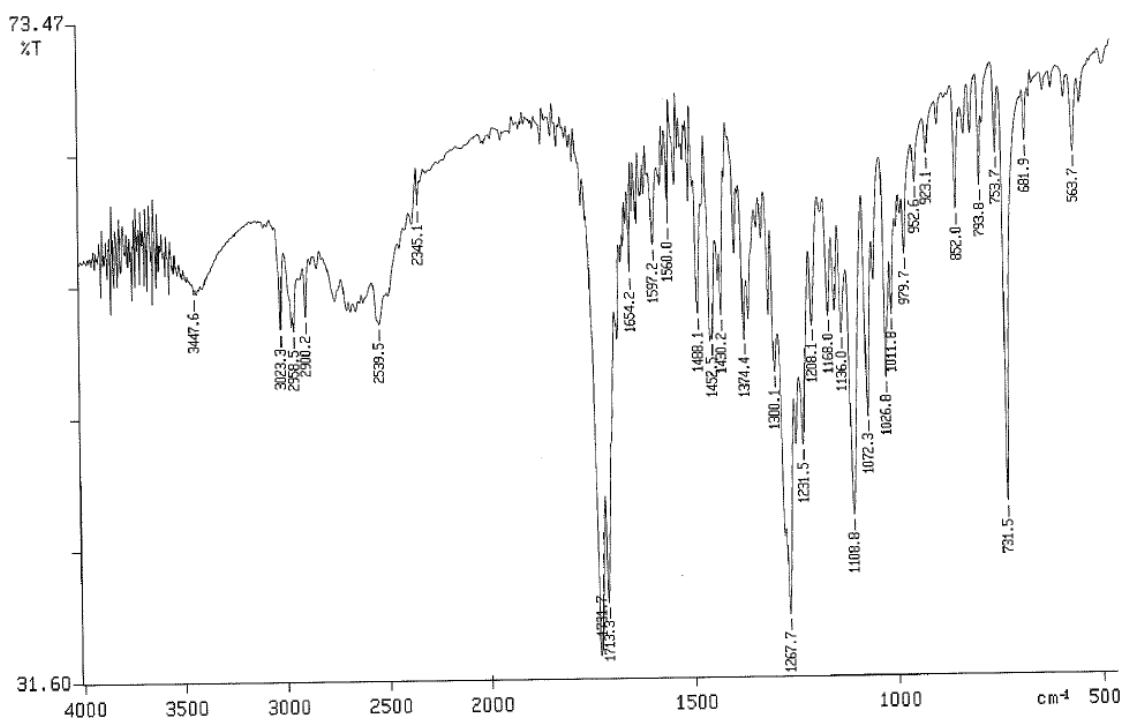
4.2.3. Infra-Red spectrometry (FT-IR)

Infra-Red spectrometry (FT-IR), using the anhydrous KBr disk method, enabled all the contents to be monitored regardless of their solubility. Thus, more information can be collected to complete each samples profile.

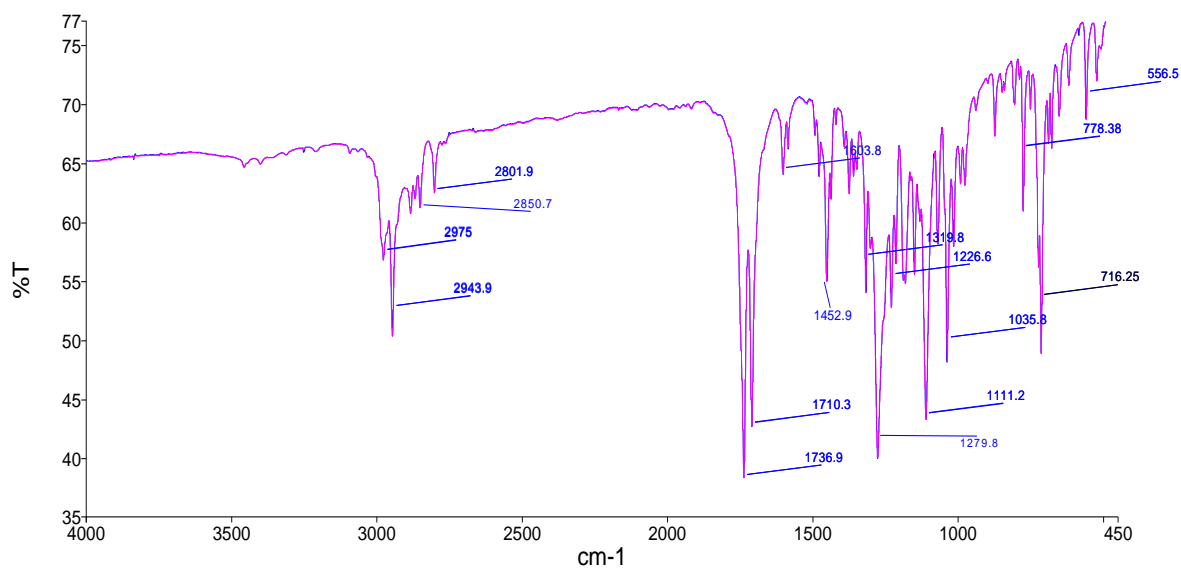
The data obtained show that FT-IR could be used to differentiate between different samples due to the diversity of peaks related to different components. The peaks in each spectrum look like a bar-code that is unique for each sample (Fig. 4.12).

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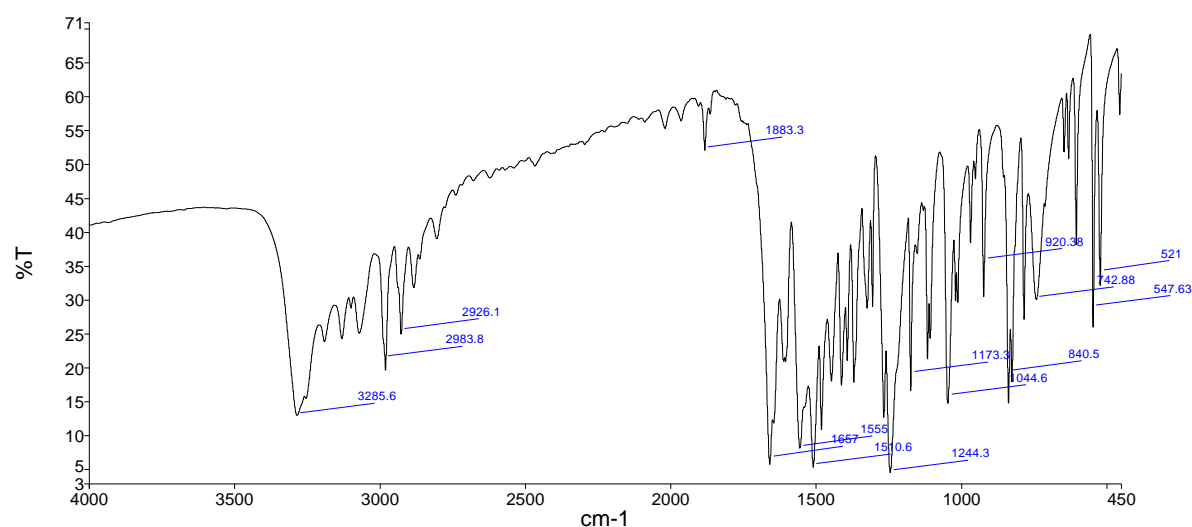
Coc. HCl



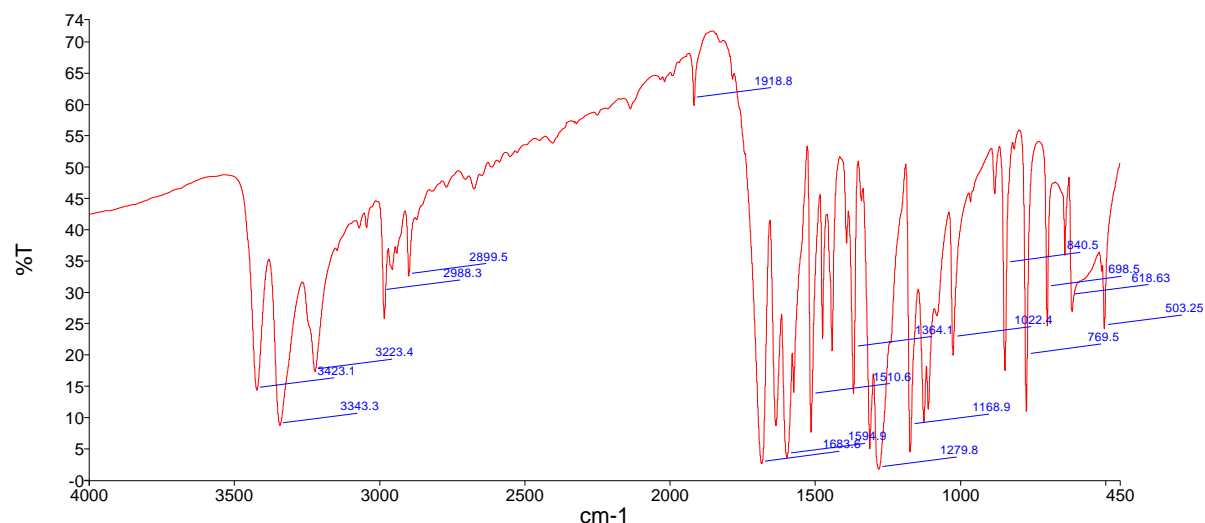
a. Cocaine HCl



b. Cocaine free-base



c. Phenacetin



d. Benzocaine

Fig. 4.12. FT-IR spectra of pure standards.

a. cocaine HCl, b. cocaine free-base, c. phenacetin, d. benzocaine

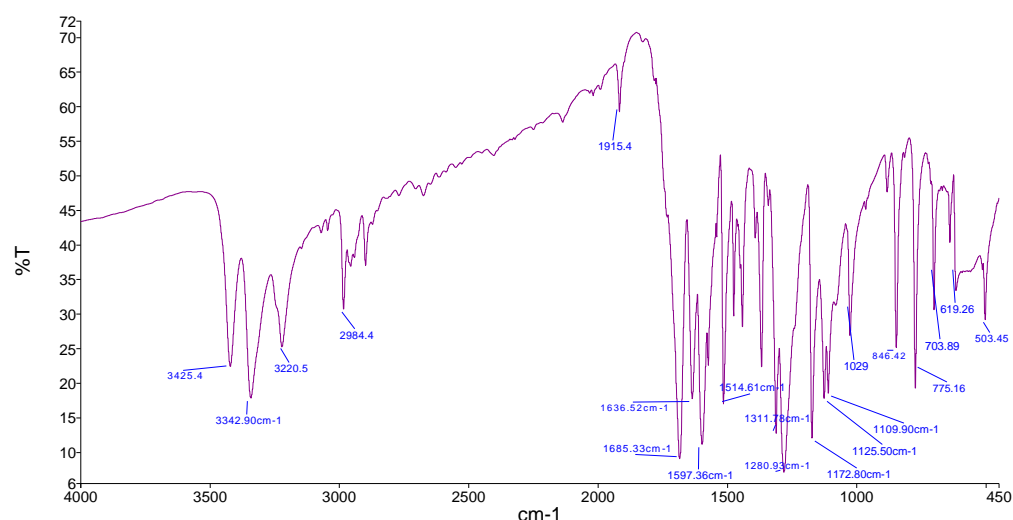
Cocaine HCl (Fig. 4.12a) has some strong bands corresponding with its functional groups and the motion of the various bonds. The most distinctive peak compared to cocaine free-base is $\sim 2539\text{ cm}^{-1}$, interpreted as the N-H stretching due to the HCl salt formation. The strong bands at 1713 and 1731 cm^{-1} are attributed to the stretching vibration of the two carbonyl groups. The stretching bands of C-O are around 1108 , 1231 , and 1267 cm^{-1} . The bands of mono-substituted benzene stretching are around 1026 and 1072 cm^{-1} . While cocaine free-base (Fig. 4.12b) showed similar strong bands with small shifts compared with cocaine HCl bands at

1736, 1710, 1279, 1226, 1111, 1035, and 716 cm^{-1} , this last one a C-H out-of-plane bending of the benzyl group. The appearance of bands of intermediate intensity is between 3000 and 2800 cm^{-1} and the most intense peak is around 2943 cm^{-1} .

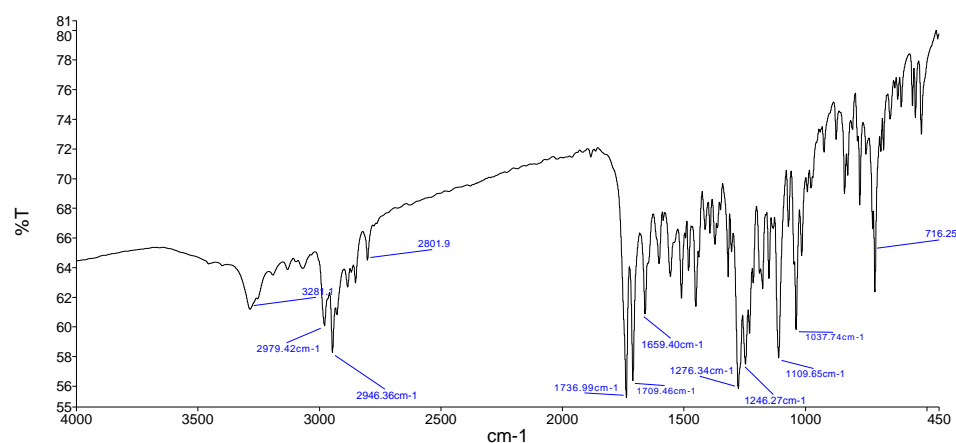
The phenacetin FT-IR spectrum (Fig. 4.12c) showed characteristic bands in the range between 2926 and 3285 cm^{-1} . The single intensive and slightly wide band at 3285 cm^{-1} is attributed to an amide group attached to an aromatic ring (Ar-NH-CO-). The aromatic C-H bands are around 3000 and 3200 cm^{-1} , those at 2926 and 2983 cm^{-1} refer to CH_3 and CH_2 , and bands at 1244 and 1044 cm^{-1} are attributed to C (Ar)-O-C stretching (symmetric, asymmetric).

The benzocaine FT-IR spectrum (Fig. 4.12d) showed the characteristic bands of an amino group (NH_2) at 3423-3223 cm^{-1} , the band for aromatic C-H stretching at 2988 cm^{-1} , the carbonyl band at 1683 cm^{-1} , C-O stretching at 1279 cm^{-1} , and alkane C-H bands at 1168 and 840 cm^{-1} .

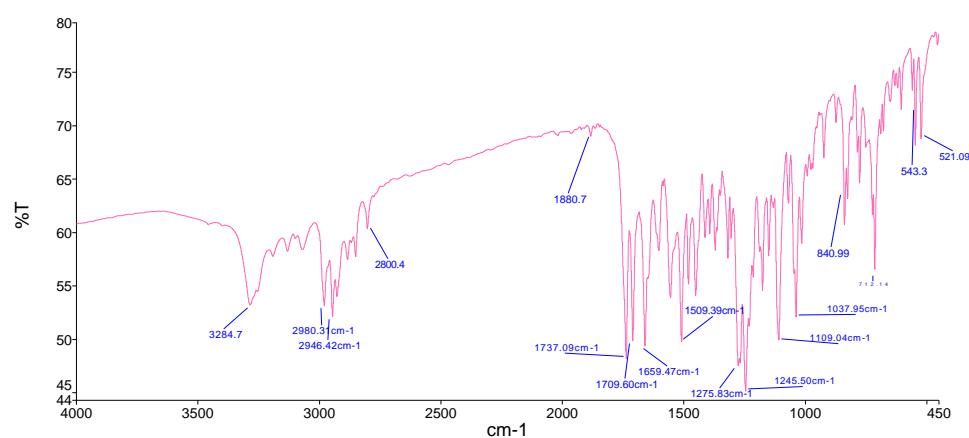
FT-IR spectra of crack samples are more complex compared with the spectra of authentic compounds and have more overlapped bands (Fig. 4.13). A qualitative analysis of crack cocaine samples by visual inspection is difficult due to overlapping of peaks in the spectra. It could be useful to identify some unique bands attributed to cocaine or other compounds, while it is not easy if the case of many cutting agents are used or the concentration of one of the cutting agents is high or drug is low. This is the case of sample 2931657 C where it looks identical to pure benzocaine. Indeed, it contains less than 10 % of cocaine. On the other hand, the FT-IR spectra can be used to carry out further statistical analysis, e.g. PCA, hierarchical cluster analysis (HCA), and Partial Least Squares (PLS) [52].



a. Crack sample 2931657 C



b. Crack sample 2932658 B



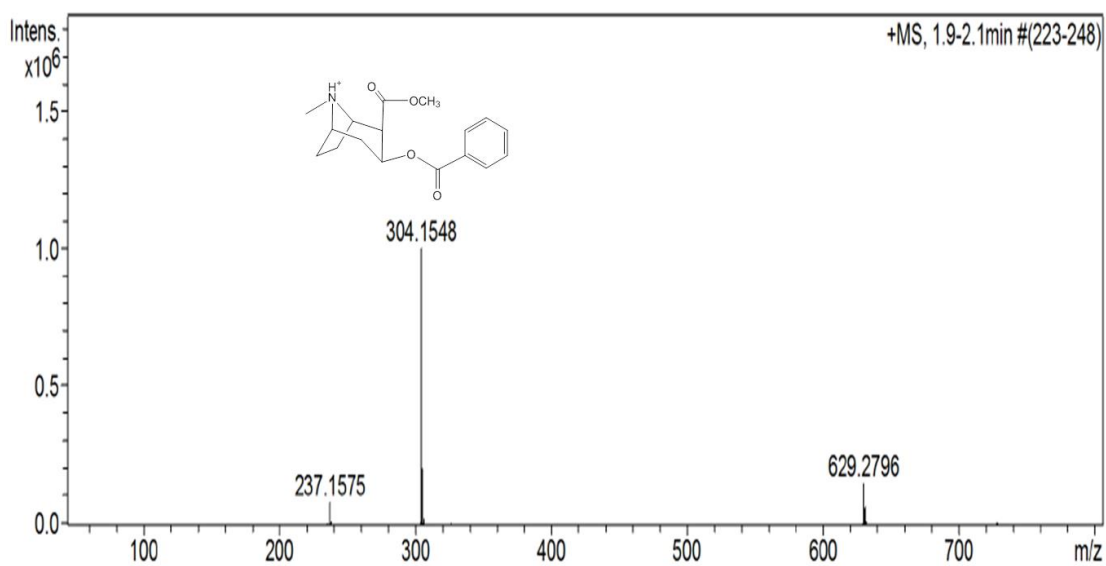
c. Crack REF sample (cocaine base and phenacetin)

Fig. 4.13. FT-IR spectra of different crack samples.

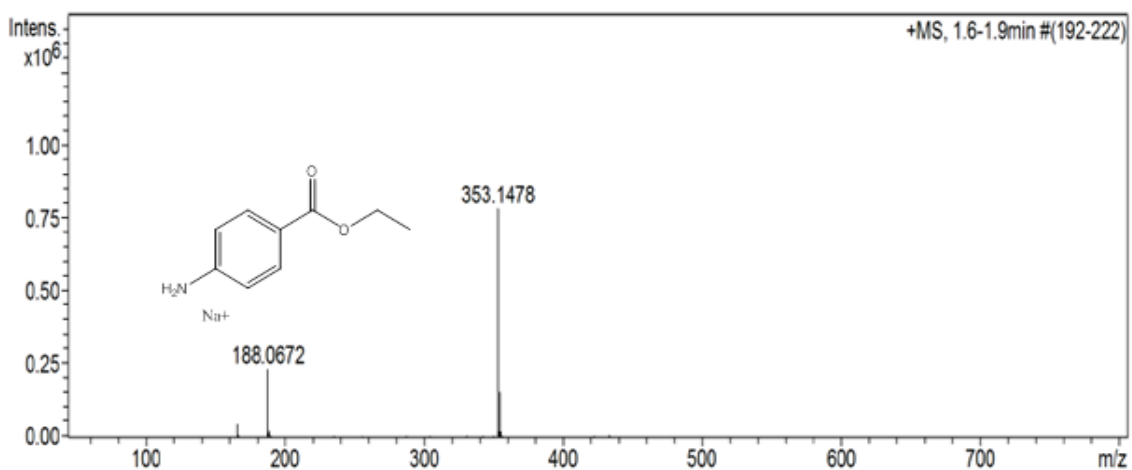
For lay drug-users, the complexity of the IR spectra, even of pure components, will reduce the impact of these data in conveying the idea of what if any impurities are present in their drugs.

4.2.4. Mass Spectrometry (MS)

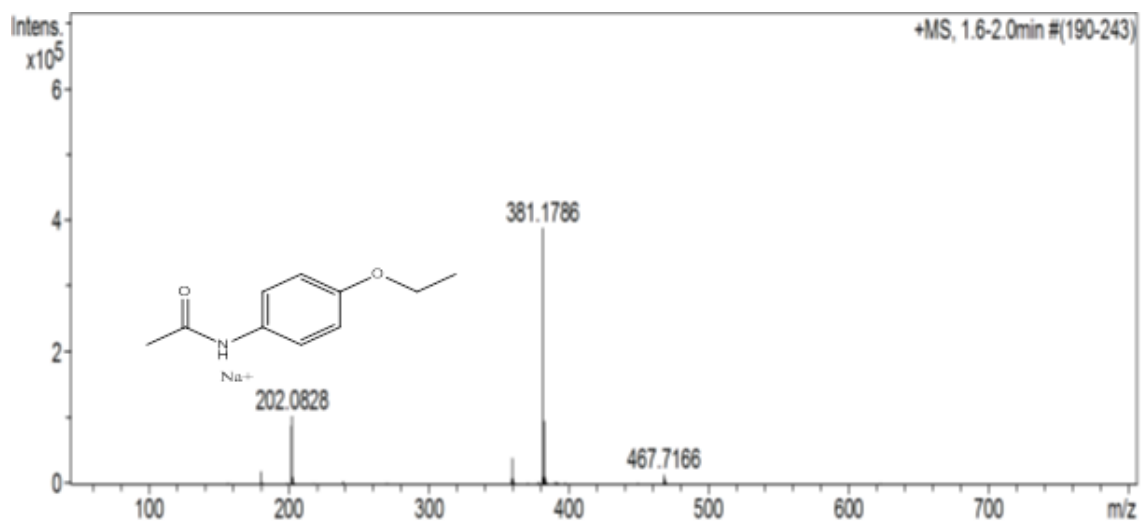
Crack cocaine (1-3 mg) was dissolved in methanol, and then the sample was analysed by high-resolution electrospray ionisation mass spectrometry (HR ESI MS). The pseudo-molecular ions of components could be helpful to profile the samples. Standard samples are presented in Fig. 4.14.a, while the samples which contained cocaine and other impurities (phenacetin and benzocaine respectively) are presented in Fig. 4.14.b.



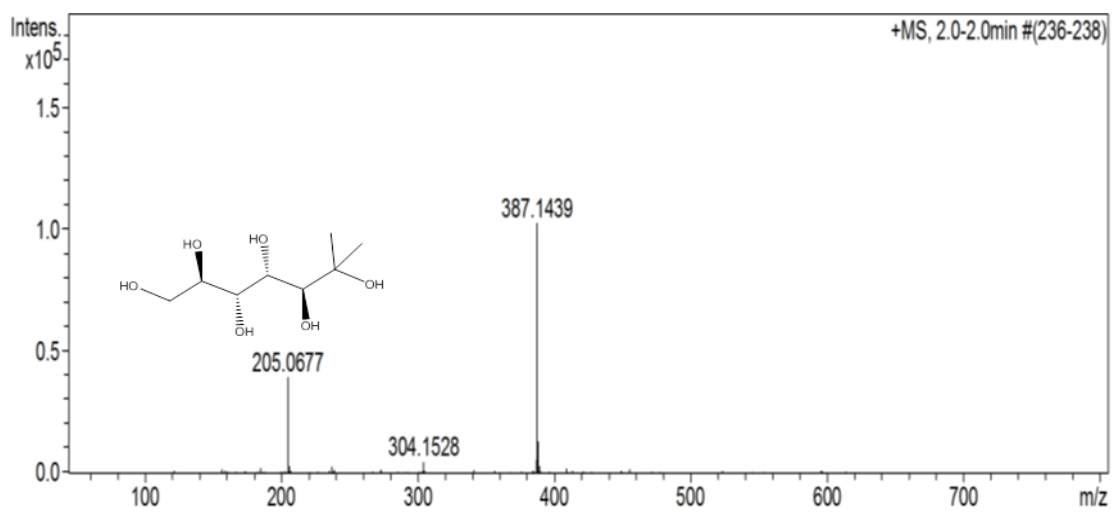
A. Cocaine base



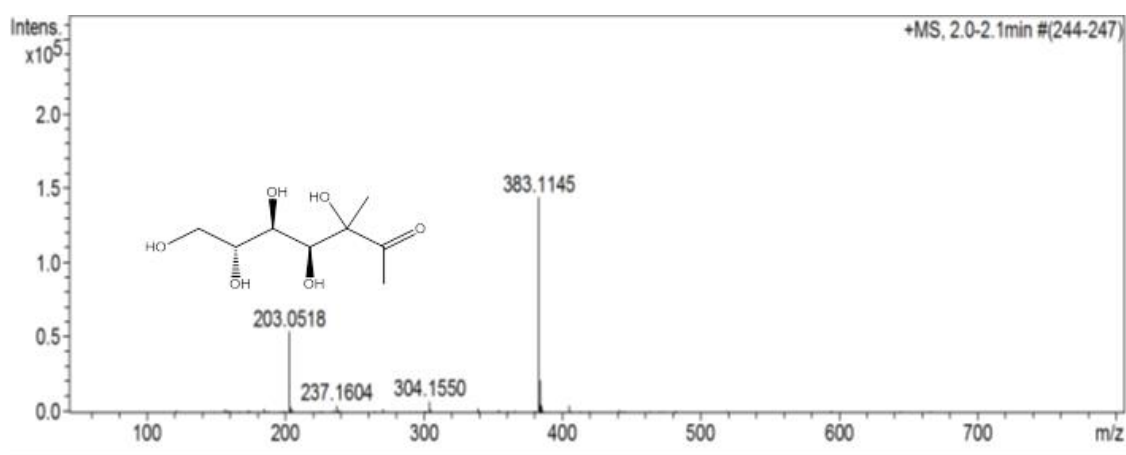
B. Benzocaine



C. Phenacetin

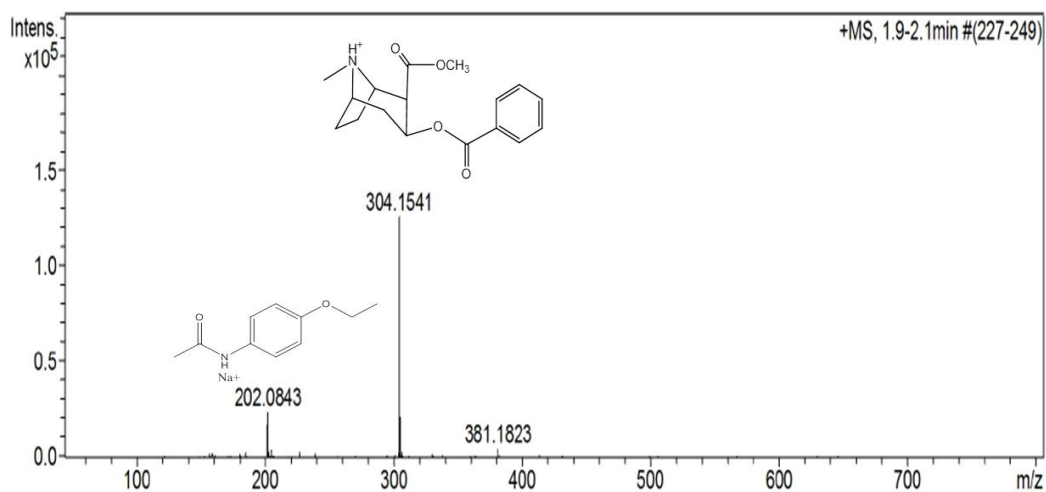


D. Mannitol

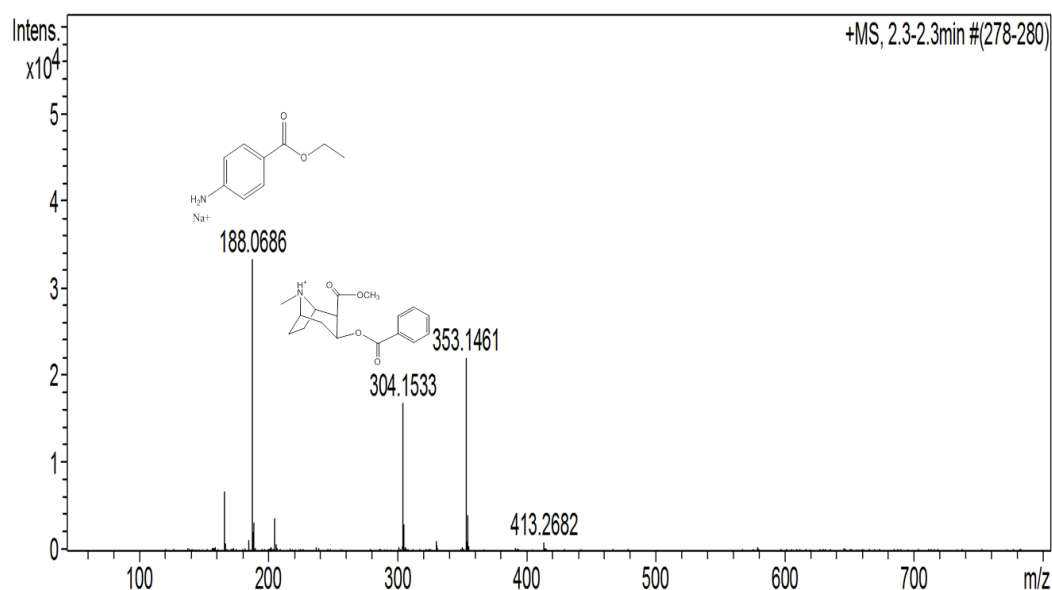


E. Glucose

- a. MS spectra for (a) cocaine base, (b) benzocaine, (c) phenacetin, (d) mannitol, (e) glucose.



(1) Crack sample 2931658b



(2) Crack 2932657a

b. MS spectra for crack samples: (1) crack sample 2931658b, (2) crack 2932657a

Fig. 4.14. MS of authentic standards and crack samples.

There are wide applications for using MS for forensic or biological analysis of cocaine, impurities, and metabolites [18, 69]. MS can provide accurate information about the molecular weight of the compounds present. MS can also give more information about the by-products of the preparation process or any degradation during storage.

4.3. Quantitative analysis

Sensitive and quantitative analytical methods are required to complete the profiling process for more details about the contents and the quantity of each component. Although there are some studies aimed at quantifying the contents by spectroscopic experiments [70], chromatographic separations were used in this project to quantify the content of the crack samples. The same samples qualified by previous spectrometric and chromatographic experiments were quantified by different techniques to obtain confirmation of the results.

4.3.1. High Performance Liquid Chromatography (HPLC)

Optimization of HPLC system

The mobile phases were optimised to obtain high resolution between phenacetin and benzocaine primarily, as cocaine was generally well resolved from those two cutting agents.

Mobile phase 1 was successful in identifying and measuring paracetamol. The HPLC-UV did not reveal any significant peaks for phenacetin, even at high concentrations. The observed results included a small broad peak two to three minutes after the injection point; it may be a degradation product. A possible explanation for a lack of a phenacetin peak could be that the phenacetin is strongly retained on the column. Paracetamol was only resolved by this mobile phase. More organic modifier was used, but sufficient resolution was not achieved. Mobile phase 2 failed to show a peak for phenacetin. Paracetamol did not afford any peaks with mobile phase 3. Peaks were obtained from benzocaine, procaine, and phenacetin, but their retention times were very close together, and difficulties would arise when attempting to distinguish between the peaks when testing crack samples.

Mobile phase 4, with its increased proportion of the aqueous solvent, was introduced in an attempt to increase the retention time of the components, especially phenacetin. Mobile phase 5 gave a better set of results, the resolution between benzocaine and phenacetin was much greater. Mobile phases 6 and 7 did not give resolved peaks between cocaine and other cutting agents. Mobile phases 8 and 9 showed better resolution than previous mobile phases. Mobile phase 9 was used as the mobile phase in the crack cocaine analysis protocol (K' cocaine = 5.99), other retention factors for cutting agents were 1.2 and 2.25 for phenacetin and benzocaine, respectively (Table 4.5). Calibration curves of cocaine free-base, cocaine HCl, phenacetin, benzocaine, and procaine were determined.

Retention factor K' , previously called the partition factor or capacity factor, is calculated by following equation:

$$K' = (t_R - t_0)/t_0$$

where K' : retention factor; t_R : retention time of elute; t_0 : retention time of mobile phase.

Table 4.5

Optimization of HPLC mobile phase

| System | Composition |
|--------|---|
| 1 | (140:0.8:800) MeOH: formic acid: potassium dihydrogen phosphate |
| 2 | (200:1:800) MeOH: formic acid: potassium dihydrogen phosphate |
| 3 | (480:120:430:0.5) H ₂ O: THF: MeOH: TEA |
| 4 | (500:120:430:0.5) H ₂ O: THF: MeOH: TEA |
| 5 | (510:120:400:0.5) H ₂ O: THF: MeOH: TEA |
| 6 | (540:1:1000) Isopropyl alcohol: formic acid: potassium dihydrogen phosphate |
| 7 | (550:120:360:0.5) H ₂ O: THF: MeOH: TEA |
| 8 | (400:1:400) MeOH: formic acid: potassium dihydrogen phosphate |
| 9 | (700:430:70:0.5) H ₂ O: MeCN: THF: TEA |

Calibration curve of cocaine hydrochloride**Table 4.6**

HPLC results of cocaine HCl to prepare the calibration curve

| Cocaine HCl (mg/mL) | R.T. (min) | AUC |
|---------------------|------------|----------|
| 0.050 | 10.038 | 2638745 |
| | 10.028 | 2646609 |
| 0.100 | 10.041 | 5867025 |
| | 10.034 | 5746259 |
| 0.200 | 10.012 | 11296928 |
| | 10.014 | 11096179 |
| | 9.991 | 11230490 |
| 0.400 | 9.968 | 21783033 |
| | 9.986 | 21948697 |
| | 9.976 | 21745359 |
| 0.600 | 9.972 | 31994122 |
| | 9.971 | 31825272 |
| | 10.006 | 32351009 |
| Average | 10.004 | |
| ST deviation | 0.026 | |

AUCs at each concentration were calculated and they were used to draw the calibration curve (Table 4.6). The results were plotted (Fig. 4.15).

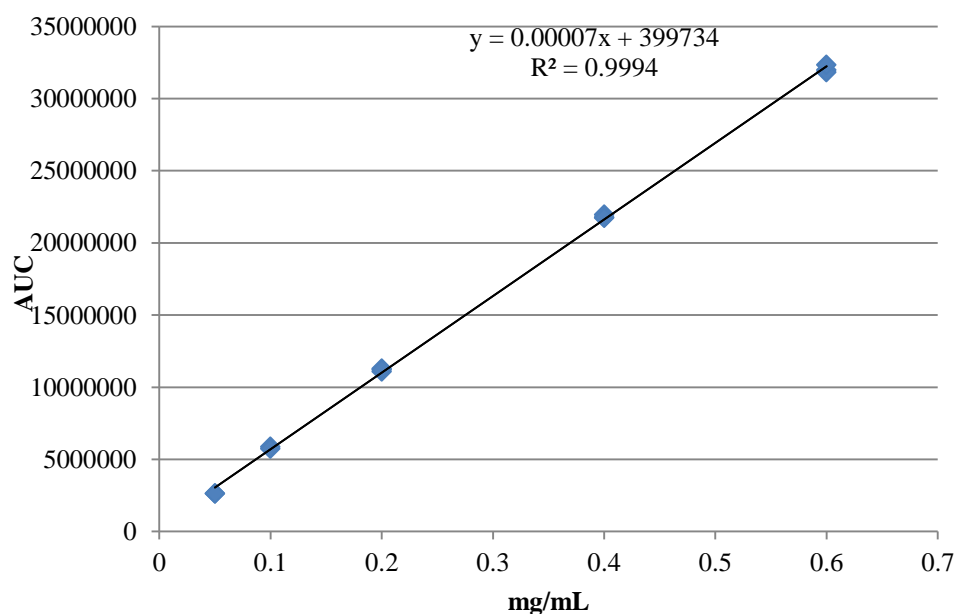


Fig. 4.15. Calibration curve of cocaine HCl by HPLC.

Calibration curve of cocaine free-base

AUCs at each concentration were calculated and they were used to draw the calibration curve (Table 4.7). The results were plotted (Fig. 4.16).

Table 4.7

HPLC results of cocaine free-base to prepare the calibration curve

| Cocaine base conc (mg/mL) | R.T. (min) | AUC |
|------------------------------|------------|---------|
| 0.05 | 9.964 | 2670037 |
| | 9.960 | 2750463 |
| | 9.961 | 2677953 |
| 0.1 | 9.964 | 5758462 |
| | 9.957 | 5641832 |
| | 9.961 | 5205248 |

| | | |
|---------|--------|----------|
| 0.2 | 9.963 | 11198652 |
| | 9.958 | 11250419 |
| | 9.966 | 10640469 |
| 0.4 | 9.975 | 20432831 |
| | 9.980 | 21532974 |
| | 9.983 | 20517210 |
| 0.6 | 10.000 | 28501242 |
| | 9.994 | 32412571 |
| | 10.099 | 25758200 |
| average | 9.979 | |

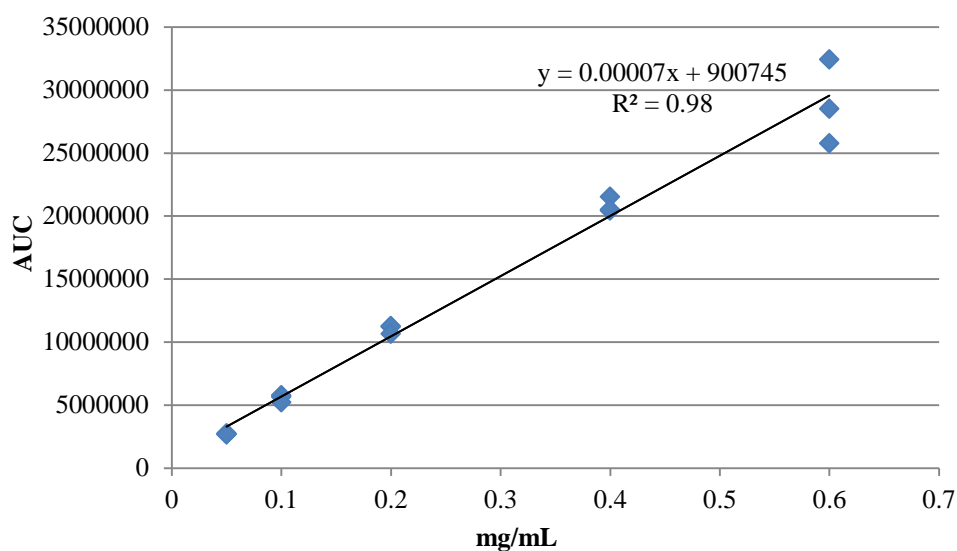


Fig. 4.16. Calibration curve of cocaine free-base by HPLC.

Calibration curve of phenacetin

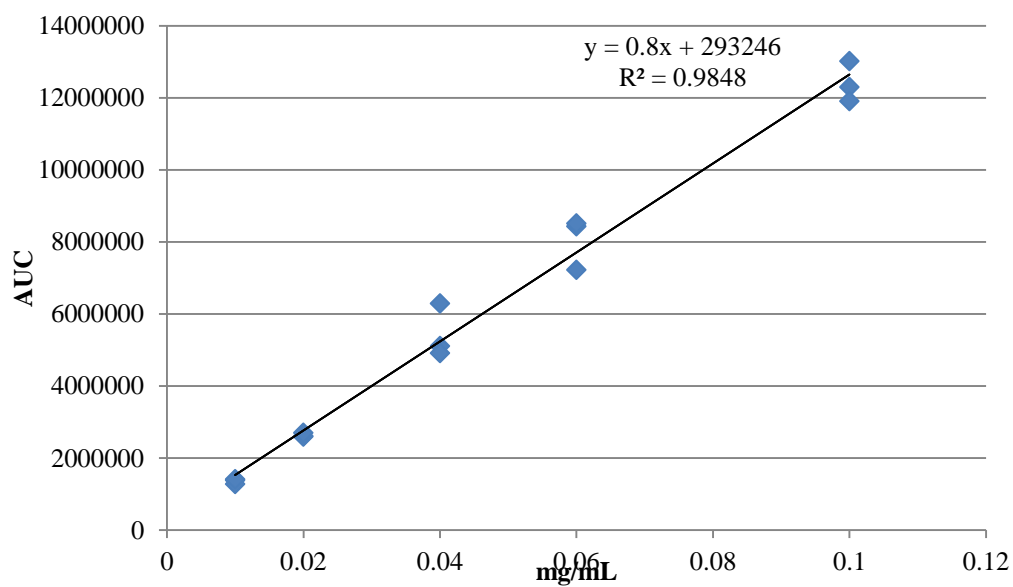
Low concentration calibration curve of phenacetin

AUCs at each concentration were calculated and they were used to draw the calibration curve (Table 4.8). The results were plotted (Fig. 4.17).

Table 4.8

HPLC results of phenacetin to prepare the calibration curve (low concentrations)

| low concentration of phenacetin | R.T. (min) | AUC |
|---------------------------------|------------|----------|
| 0.01 | 3.28 | 1378222 |
| | 3.27 | 1276137 |
| | 3.26 | 1410660 |
| 0.02 | 3.26 | 2594158 |
| | 3.26 | 2612599 |
| | 3.25 | 2700916 |
| 0.04 | 3.25 | 5106576 |
| | 3.25 | 6289793 |
| | 3.25 | 4911458 |
| 0.06 | 3.25 | 8428212 |
| | 3.24 | 7221120 |
| | 3.25 | 8510569 |
| 0.1 | 3.24 | 12294368 |
| | 3.24 | 13014965 |
| | 3.24 | 11900233 |

**Fig. 4.17.** Calibration curve of phenacetin by HPLC (low concentrations).

High concentration calibration curve of phenacetin

AUCs at each concentration were calculated and they were used to draw the calibration curve (Table 4.9). The results were plotted (Fig. 4.18). Two calibration curves for phenacetin were required to measure phenacetin in both aqueous and organic layers in the case of the extraction using protocol A.

Table 4.9

HPLC results of phenacetin to prepare the calibration curve.

| concentration of phenacetin | R.T. (min) | AUC |
|-----------------------------|------------|----------|
| 0.01 | 3.3014123 | 1472232 |
| | 3.3183316 | 1622633 |
| | 3.3155939 | 1615611 |
| 0.05 | 3.247936 | 5976392 |
| | 3.99075 | 76140 |
| | 3.2409261 | 5585441 |
| 0.1 | 3.2529722 | 12003947 |
| | 3.2472277 | 12327884 |
| | 3.2573815 | 11908028 |
| 0.2 | 3.2448333 | 23857594 |
| | 3.2581667 | 24043838 |
| | 3.2531667 | 23934505 |
| 0.4 | 3.1848333 | 36922377 |

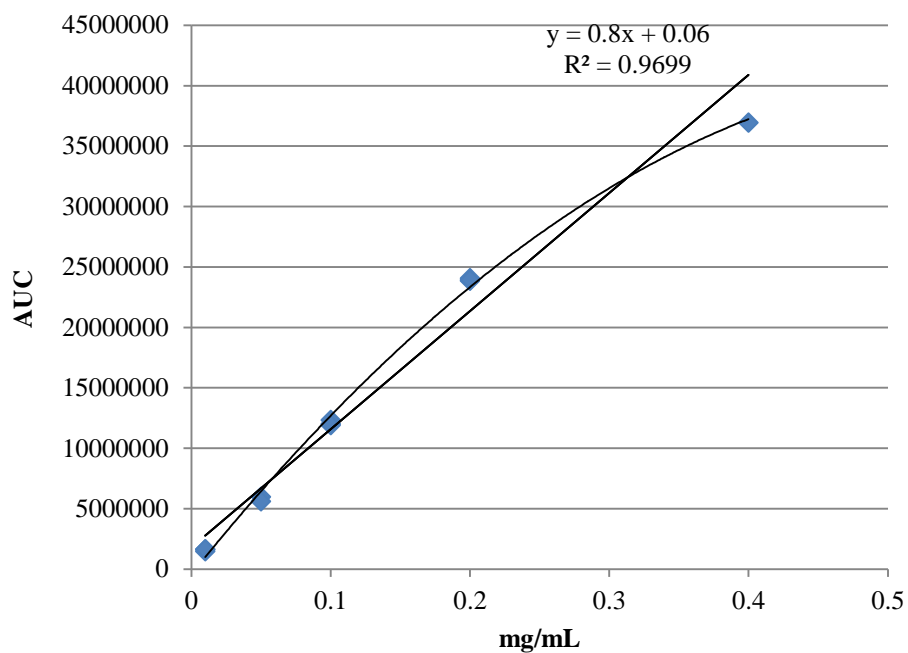


Fig. 4.18. Calibration curve of phenacetin by HPLC.

Benzocaine calibration curve

AUCs at each concentration were calculated and they were used to draw the calibration curve (Table 4.10). The results were plotted (Fig. 4.19).

Table 4.10

HPLC results of benzocaine to prepare the calibration curve

| benzocaine conc mg/mL | R.T. (min) | AUC |
|-----------------------|------------|----------|
| 0.01 | 4.69 | 1536594 |
| | 4.69 | 1493760 |
| | 4.69 | 1493760 |
| 0.05 | 4.68 | 8171433 |
| | 4.69 | 8148912 |
| | 4.69 | 8130180 |
| 0.1 | 4.66 | 16383710 |
| | 4.81 | 16651348 |
| | 4.82 | 17403726 |
| 0.2 | 4.67 | 32449158 |
| | 4.67 | 30414870 |
| | 4.73 | 31855212 |

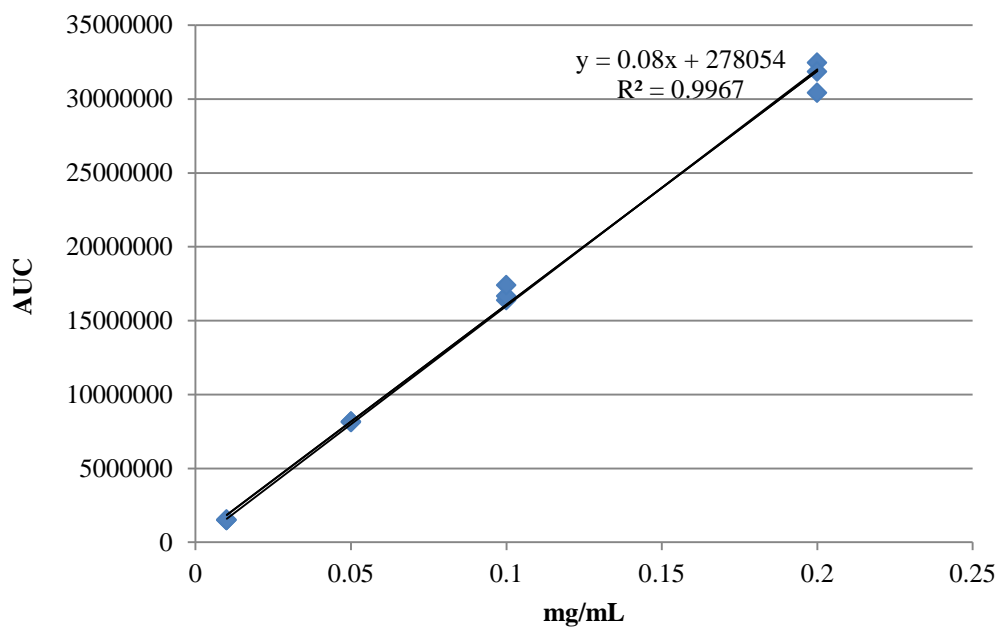


Fig. 4.19. Calibration curve of benzocaine by HPLC.

Procaine calibration curve

AUCs at each concentration were calculated and they were used to draw the calibration curve (Table 4.11). The results were plotted (Fig. 4.20).

Table 4.11

HPLC results of procaine to prepare the calibration curve.

| procaine concentration | R.T. (min) | AUC |
|------------------------|---------------|----------|
| 0.01 | 4.70 | 1154211 |
| | 4.68 | 908559 |
| | 4.68 | 1042848 |
| 0.05 | 4.72 | 5095104 |
| | 4.71 | 4931398 |
| | 4.72 | 5254739 |
| 0.1 | 4.70 | 10777283 |
| | 4.70 | 10834751 |
| | 4.70 | 11100988 |
| 0.2 | 4.70 | 19759485 |
| | 4.71 | 20629377 |

| | | |
|-----|------|----------|
| | 4.70 | 21009982 |
| 0.3 | 4.71 | 30882830 |
| | 4.71 | 30906348 |
| | 4.69 | 28414243 |

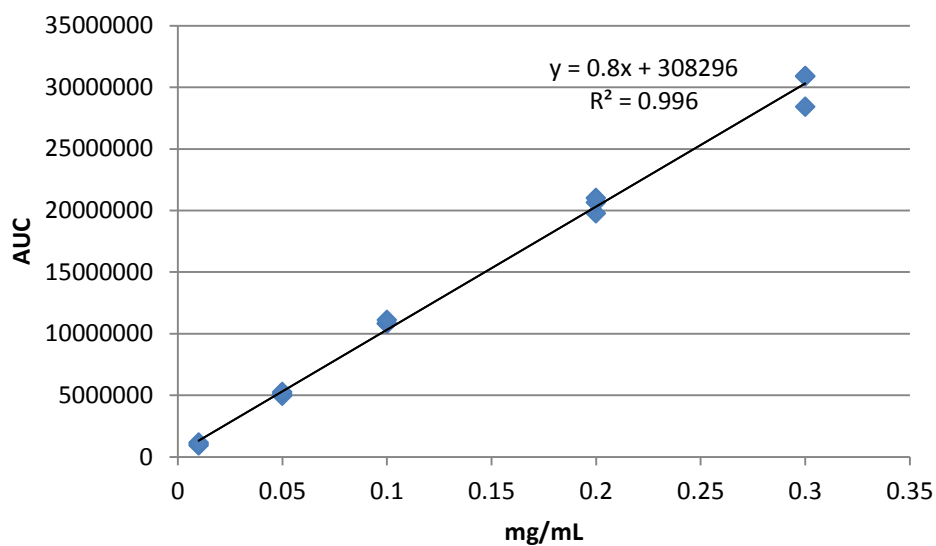


Fig. 4.20. Calibration curve procaine by HPLC.

HPLC validation

Six replicates of the crack reference sample were analysed according to the protocol to validate the analysis. One replicate was clearly in error and was discarded for the purposes of statistical analysis (Table 4.12).

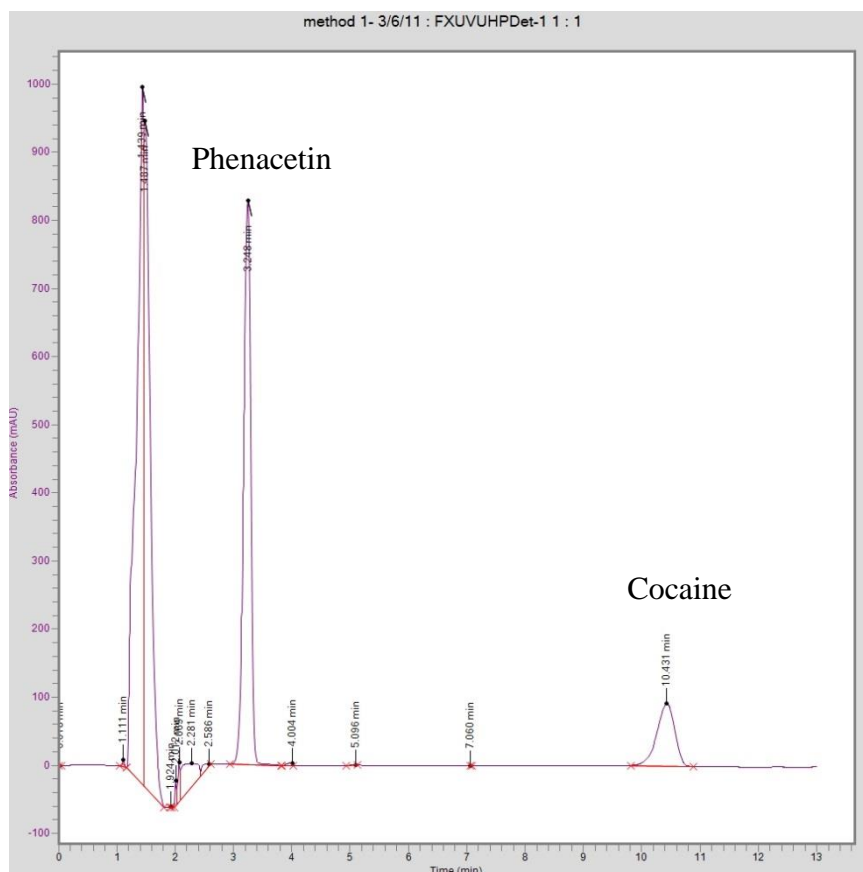
Table 4.12

HPLC method validation

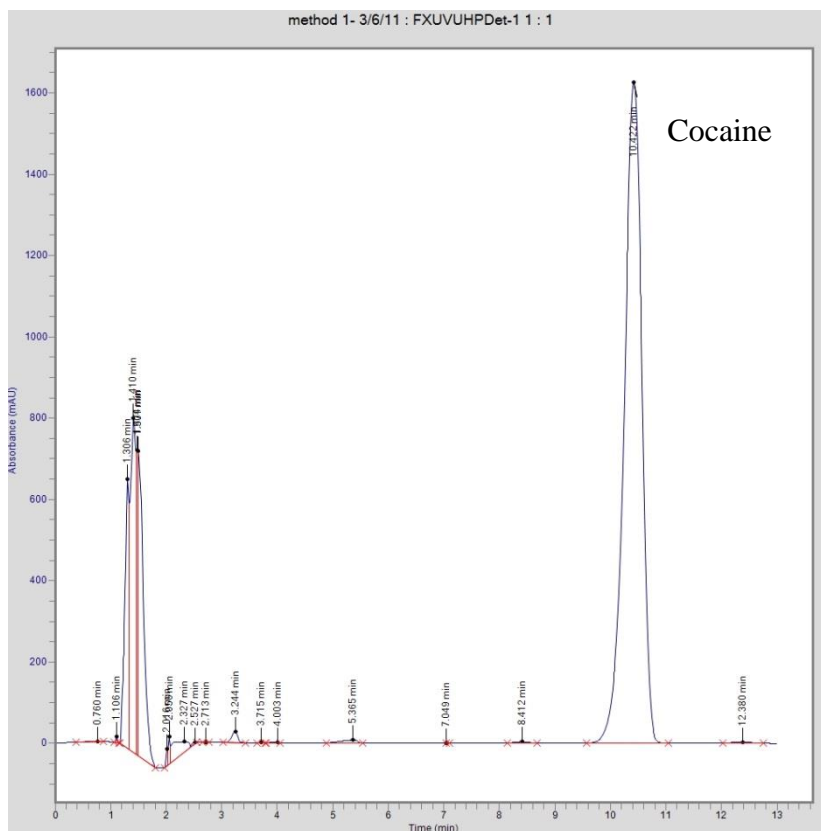
| Sample | Weight (mg) | Cocaine (%) | Phenacetin (%) |
|---------|-------------|-------------|----------------|
| Ref 1 | 60.2 | 44.4 | 32.98 |
| Ref 2 | 60.3 | 45.975 | 35.248 |
| Ref 3 | 60.1 | 47.35 | 35.91 |
| Ref 5 | 60.0 | 45.4 | 33.56 |
| Ref 6 | 60.2 | 46.6 | 35.3 |
| Average | | 45.95 | 34.60 |
| STDV | | 1.12 | 1.25 |
| RSD | | 2.45 | 3.63 |

HPLC analysis of street samples of crack cocaine

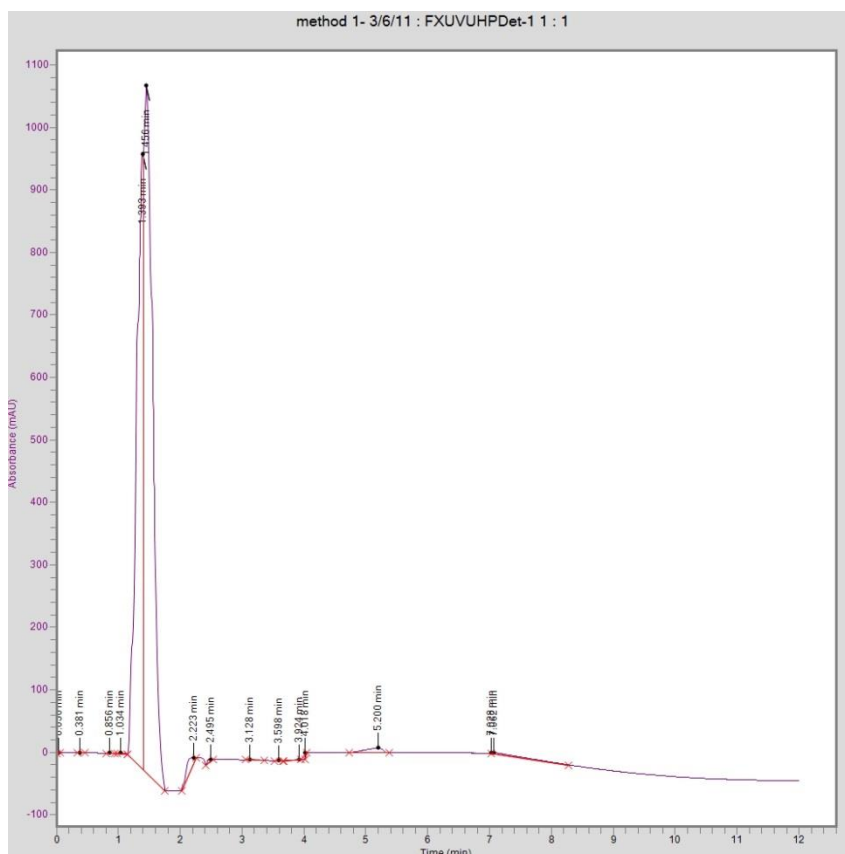
A series of 61 samples seized by the Police in Swindon in 2007 were analysed; 17 samples out of these 61 did not contain cocaine (~28 %). These samples have the following codes: F 264508 (4a, 4b, 5a, 5b, 5c, 5d, 5e, 6a, 6b, 6c, 8, 9, 10), F 264308-8, F 264308-9, F 264308-10, JGG 01768B, 202506, 190340, and Jf 604140. These 17 samples were provided as powders collected by the Police as crack while they may actually be a dust collected from the place where the crack samples were seized, or they may be fake crack samples sold to crack users as crack while they are not. In further analysis, the percentage of cocaine and phenacetin was determined for the rest of the samples (44 out of 61 crack samples) (Table 4.13). The average cocaine content $x = 33\%$ in the DCM layer as cocaine free-base with standard deviation $SD = 6.59$, and relative standard deviation $RSD = 20.01$. Phenacetin is the detected impurity in these samples in the DCM layer $x = 44.5\%$, $SD = 14.3$, and $RSD = 32.17$. Although the average percentage of crack samples was ~35, while the maximum amount of cocaine was 61.1 % in single sample (JG 600323-2) that may be a sample that is going to be cut with other cutting agents later or it came from a purer batch of crack samples. This sample did not contain any cutting agent besides cocaine, and this was confirmed by NMR spectroscopy that showed cocaine as the only compound in this samples Fig 4.11. This can give evidence for the importance of profiling procedures and using more than one technique to collect more information about the seized samples and confirm the results by more than one analytical technique. Phenacetin was the cutting agent which was detected in the analysed samples in 43 samples out of 61 (69 %). The maximum amount of phenacetin was 86.76 % (F 314608-7.1). The following HPLC chromatograms (Fig. 4.21) show the variation between three different crack samples. The first sample (Sample JG600323-1) is an example of a crack sample that contained a mixture of cocaine free-base and phenacetin, while the second sample (Sample JG600323-2) contains only cocaine free-base that had the maximum cocaine of all the samples analysed and the purity was confirmed by NMR spectroscopy. The third sample (sample JF604140) is negative in cocaine content, also phenacetin was not identified in this sample.



1. Sample JG600323-1



2. Sample JG600323-2



3. Sample JF604140

Fig. 4.21. HPLC chromatograms of seized crack samples.

Table 4.13

Quantitative results of analysis of crack samples by HPLC

| Sample number | HPLC DCM layer (%) | | HPLC D ₂ O layer (%) | | Total | |
|---------------|--------------------|------------|---------------------------------|------------|---------|------------|
| | cocaine base | phenacetin | cocaine HCl | phenacetin | cocaine | phenacetin |
| F 264508-1a | 33.66 | 32.32 | 0.22 | 1.12 | 33.87 | 33.44 |
| F 264508-1f | 35.26 | 33.75 | 0.18 | 1.03 | 35.44 | 34.78 |
| F 264508-1i | 38.25 | 34.57 | 0.48 | 1.01 | 38.73 | 35.58 |
| F 264508-1k | 33.57 | 40.90 | 0.00 | 1.20 | 33.57 | 42.10 |
| F 264508-1s | 34.73 | 40.77 | 0.06 | 1.33 | 34.79 | 42.10 |
| F 264508-1w | 34.16 | 39.95 | 0.19 | 1.38 | 34.35 | 41.33 |
| F 264508-1y | 24.81 | 36.90 | 0.04 | 1.26 | 24.85 | 38.16 |
| F 264508-1bb | 27.58 | 36.09 | 0.09 | 1.20 | 27.67 | 37.30 |
| F 264508-1hh | 32.43 | 44.02 | 0.02 | 1.13 | 32.45 | 45.16 |
| F 264508-1kk | 32.66 | 43.57 | 0.12 | 1.29 | 32.78 | 44.87 |

| | | | | | | |
|--------------|-------|-------|------|------|-------|-------|
| F 263408 2a | 34.96 | 42.69 | 0.24 | 1.32 | 35.20 | 44.01 |
| F 263408 2e | 35.04 | 44.24 | 0.52 | 1.73 | 35.56 | 45.96 |
| F 263408 2h | 35.18 | 45.32 | 0.08 | 1.32 | 35.27 | 46.64 |
| F 263408 2k | 35.59 | 46.35 | 0.11 | 1.23 | 35.70 | 47.58 |
| F 263408 2p | 33.21 | 42.54 | 0.08 | 1.21 | 33.29 | 43.74 |
| F 263408-2s | 33.23 | 46.31 | 0.05 | 1.34 | 33.28 | 47.66 |
| F 263408-2v | 30.64 | 43.23 | 0.10 | 1.31 | 30.75 | 44.54 |
| F 263408-2z | 34.38 | 41.78 | 0.10 | 1.44 | 34.48 | 43.22 |
| F 263408-2ee | 34.84 | 47.44 | 0.11 | 1.43 | 34.96 | 48.87 |
| F 263408-2gg | 31.86 | 44.82 | 0.08 | 1.35 | 31.94 | 46.16 |
| F263408-3C | 35.77 | 41.52 | 0.32 | 1.21 | 36.09 | 42.73 |
| F263408-3 g | 33.84 | 41.73 | 0.10 | 1.07 | 33.94 | 42.80 |
| F263408-3 j | 35.72 | 42.90 | 1.19 | 2.39 | 36.91 | 45.28 |
| F263408-3q | 34.63 | 47.41 | 0.11 | 1.34 | 34.74 | 48.76 |
| F263408-3L | 34.02 | 45.90 | 0.16 | 1.37 | 34.18 | 47.27 |
| F263408-3t | 33.92 | 46.95 | 0.10 | 1.25 | 34.02 | 48.20 |
| F263408-3x | 32.52 | 48.37 | 0.06 | 1.36 | 32.58 | 49.73 |
| F263408-3bb | 34.76 | 45.05 | 0.07 | 1.15 | 34.83 | 46.21 |
| F263408-3jj | 33.73 | 47.38 | 0.06 | 1.25 | 33.79 | 48.63 |
| F263408-3mm | 31.99 | 44.90 | 0.15 | 1.50 | 32.14 | 46.41 |
| F 314608-7.1 | 20.37 | 86.97 | 0.12 | 2.79 | 20.49 | 89.76 |
| F 314608-7.2 | 33.80 | 58.68 | 0.19 | 1.84 | 33.99 | 60.53 |
| F 314608-7.3 | 40.56 | 73.91 | 0.39 | 2.08 | 40.96 | 75.99 |
| F 314608-7.4 | 34.56 | 40.47 | 0.05 | 1.08 | 34.62 | 41.54 |
| F 314608-7.5 | 34.12 | 41.02 | 0.07 | 1.44 | 34.18 | 42.46 |
| F 314608-7.6 | 20.12 | 53.36 | 0.01 | 1.49 | 20.13 | 54.85 |
| F 314608-7.8 | 31.86 | 44.50 | 0.00 | 1.31 | 31.86 | 45.81 |
| F 264308-7a | 34.27 | 67.30 | 0.08 | 1.98 | 34.35 | 69.28 |
| F 264308-7b | 35.49 | 69.60 | 0.55 | 2.71 | 36.03 | 72.31 |
| JGG 01768A | 25.28 | 51.02 | 0.19 | 1.71 | 25.47 | 52.73 |
| JG 600323-1 | 26.53 | 49.99 | 0.22 | 1.79 | 26.75 | 51.78 |
| JG 600323-2 | 61.10 | 0.00 | 0.92 | 0.00 | 62.03 | 0.00 |

| | | | | | | |
|-----------|-------|-------|--------|-------|-------|-------|
| 190340 | 13.97 | 0.23 | 28.99 | 0.03 | 42.95 | 0.26 |
| F 0867-08 | 27.57 | 39.51 | 0.27 | 1.27 | 27.84 | 40.78 |
| average | 32.88 | 44.46 | 0.85 | 1.39 | 33.72 | 45.85 |
| STDV | 6.59 | 14.30 | 4.35 | 0.50 | 6.21 | 14.75 |
| RSD | 20.06 | 32.17 | 513.38 | 36.21 | 18.40 | 32.17 |

The data published by European Monitoring Centre for Drugs and Drug Addiction (EMCDDA), based on data collected in 2011, show variation in the average between different countries. It was at a maximum in Greece (61 %) while it was at a minimum in Bulgaria (22 %). The detailed data showed the average purity of crack in the UK to be 26.3 % for 1483 samples. This can give an idea about the samples analysed in this study, how close to the national average in purity (<http://www.emcdda.europa.eu/publications/drug-profiles/cocaine> accessed on 31.08.2014). Additionally, the United Nations Office on Drugs and Crime (UNODC) report in 2009 showed the difference in purity between samples which were seized by customs and in transit samples seized in the street [12]. This report clearly showed the decrease in imported cocaine to UK from 70 % in 2004 to 55 % in 2009. Furthermore, at the same time, the purity in the street decreased even faster. The street samples purity was 50 % in 2004 and became about 20 % in 2009. This was explained by an increase in dilution in the UK and a massive international traffic in cutting agents (Fig. 4.22) [12]. There is a noticeable similarity between the results in Table 4.13 and in the UNODC report, although the analysed samples are limited, as provided from only one area. The UNODC data included both forms of cocaine; while Table 4.13 showed that analysed samples mainly are free-base form. Fig. 4.22 shows the increase of dilution activities which have been carried out after importing the illicit drug into the country. This process could have occurred at different levels of the distribution chain with each dealer having little knowledge about cutting agents added either before or after. All of this increases the need to establish a database to track the changes and materials that are identified in different areas, not only to look for the distribution channels but also to inform the users and the workers with users and health care about what they may expect in emergency cases due to overdose or toxic substances.

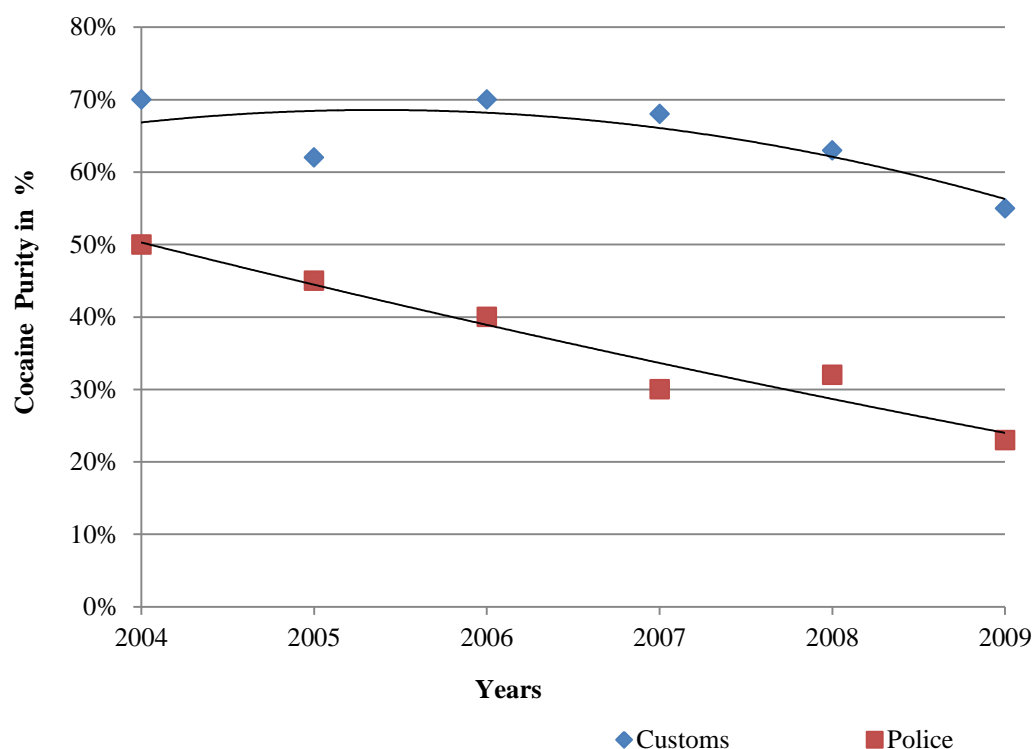


Fig. 4.22. Mean purity of cocaine seized in the UK, 2004-2009 (taken from [12]).

Concerning cocaine purity and change in illicit drug market, similar results have been reported during last few years in other European countries. Evard analysed cocaine samples were collected in 2007 from different French cities [18]. The average of cocaine was 27 % which is close to the crack samples analysed in this study. The maximum cocaine concentration was 88 % in samples analysed by Evard, while in this study it was only 66.1 % [18]. Phenacetin was identified in 54 % of French samples while it was in 69 % of the samples which were seized in Swindon, UK. Schneider and Meys [71] reported that in the 962 illicit cocaine samples they analysed, the percentage of cocaine decreased from 54.7 % in 2005 to 43.2 % in 2009. The difference between their study and the results of crack cocaine samples in this thesis is that the analysed samples in the Schneider and Meys study were seized by Police and Customs [71] while the samples in this thesis were seized by the Police only. The samples seized by Customs could be diluted again once inside the country. However, Schneider and Meys also found that phenacetin was the most common cutting agents until 2009, and since 2010 they have reported levamisole as the most plentiful adulterant in analysed cocaine samples [71].

Rodrigues [52], in 2013, reported the results of analysing 91 cocaine (free-base and salt) samples seized in 2008-2010 in Brazil. The amount of cocaine varied between 1 % and 73 %. Four adulterants (caffeine, lidocaine, benzocaine, and boric acid) were identified in their samples, but in 22 out of their 91 samples only. In comparison, in this study, the analysed samples mainly contained cocaine free-base, only a single sample of both salt and free-base forms of cocaine was identified [52]. The results can be explained as different from the results of Rodrigues due to the differences in availability. The differences of identified cutting agents and the forms of cocaine can show the importance of tracking the source and how samples seized in different countries contained different adulterants and different purity. Schifano and Corkery [72] referred to the decrease in the purity of crack samples at street level compared with the stable purity of imported crack samples. This decrease was associated with a 16-fold increase of availability between 1990-2003 [72].

4.3.2. GC-FID optimisation

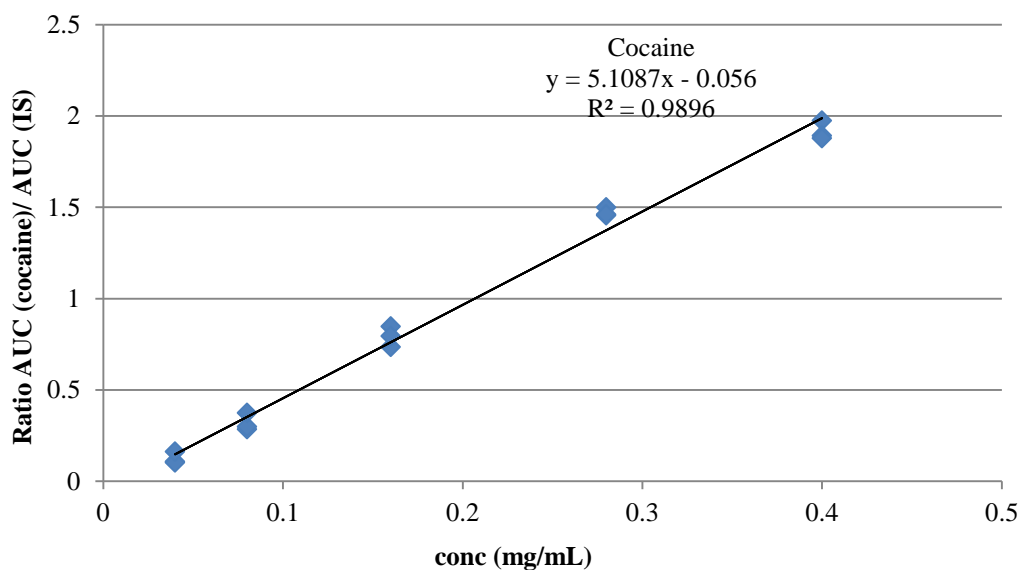
The GC-FID method was optimised to be used to analyse the products of volatising crack cocaine in a way that imitates what happens in a crack pipe to study the products that go into the users' lungs. In this way, cocaine and other low melting point compounds such as phenacetin will volatilise and be analysed by GC-FID, while other high melting point compounds and other components such as sugars will be destroyed or burn in the pipe possibly to yield other volatile products.

Optimisation of this process was carried out using the reference crack cocaine powder according the following protocol. Crack cocaine sample was dissolved in 1 mL D₂O and 1 mL of DCM. The solution was shaken for a few seconds. The DCM layer was isolated and the separation method was repeated twice using DCM (1 mL) each time. DCM (3 mL) was collected and eicosane (1 mL of a 10 % w/w solution in ethyl acetate) was added as an internal standard. The results are presented in Table 4.14. Standard solutions were prepared to plot the calibration curves for cocaine, benzocaine, and phenacetin (Fig. 4.23).

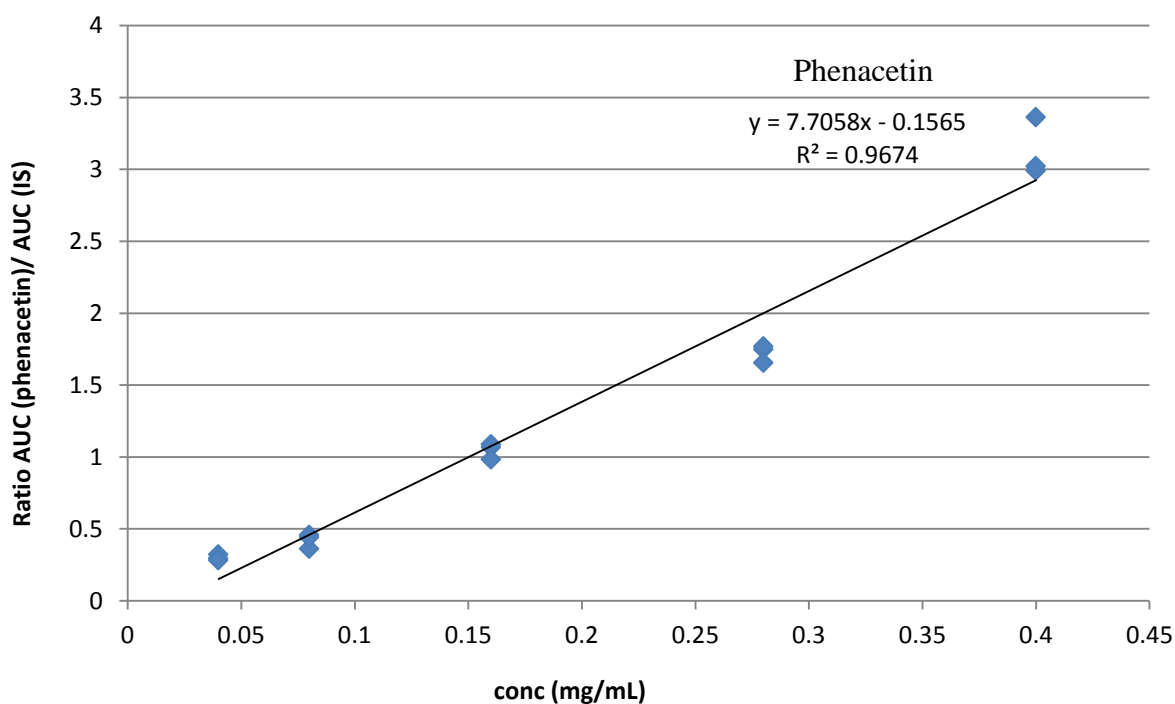
This method was used to detect the contents of crack cocaine products after volatising. Also, it could be used instead of the HPLC method to analyse crack cocaine samples. Six samples of the REF sample were analysed according to this

procedure to validate it and ensure of the collected results. The results of those replicated are presented in Table 4.15.

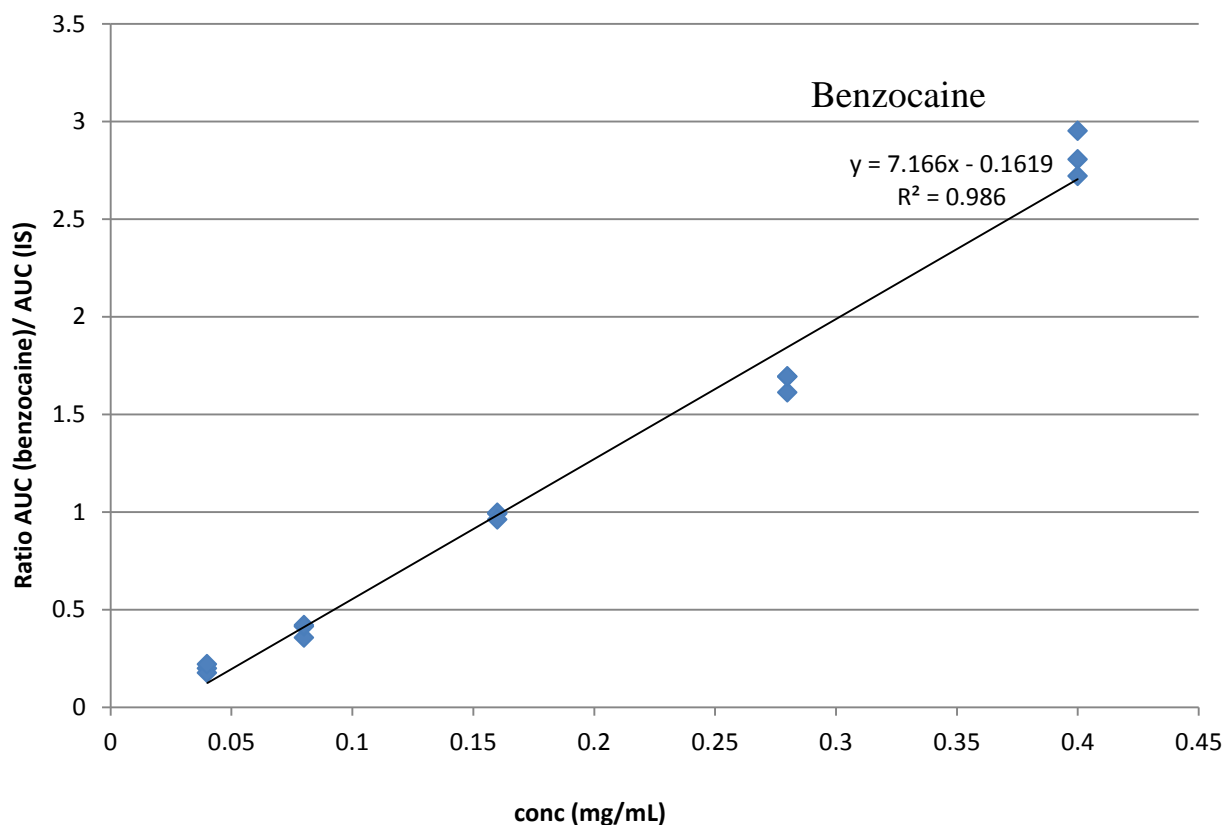
Fig. 4.24 shows the GC-FID chromatogram of a mixture solution of cocaine, benzocaine and phenacetin. The chromatogram (180 °C for 5 min, 180 to 220 °C at 8 °C/min, then hold for 10 min) obtained for 0.2 mg/mL solution of each compound showed four peaks at 5.57, 7.11, 9.05, and 15.31 min for benzocaine, phenacetin, cocaine free-base, and the internal standard (ISD, eicosane) respectively.



1. Cocaine calibration curve by GC-FID



2. Phenacetin calibration curve by GC-FID



3. Benzocaine calibration curve by GC-FID

Fig. 4.23. Calibration curves for cocaine, phenacetin, and benzocaine by GC-FID.

Table 4.14

Results of calibration curve for cocaine, phenacetin, and benzocaine by GC-FID (n = 3).

| Conc (mg/mL) | AUC I.S. | AUC Coca | Ratio Coca/IS | AUC Phen | Ratio Phen/IS | AUC Benzo | Ratio Benzo/IS |
|--------------|----------|----------|---------------|----------|---------------|-----------|----------------|
| 0.02 | 3529 | 189 | 0.0536 | 203 | 0.0575 | 224 | 0.0635 |
| 0.02 | 2812 | 163 | 0.0580 | 142 | 0.0505 | 160 | 0.0569 |
| 0.02 | 3404 | 241 | 0.0708 | 262 | 0.0770 | 254 | 0.0746 |
| 0.05 | 2869 | 419 | 0.1460 | 457 | 0.1593 | 505 | 0.1760 |
| 0.05 | 2805 | 429 | 0.1529 | 406 | 0.1447 | 502 | 0.1790 |
| 0.05 | 2829 | 385 | 0.1361 | 425 | 0.1502 | 498 | 0.1760 |
| 0.1 | 3078 | 1007 | 0.3272 | 867 | 0.2817 | 921 | 0.2992 |
| 0.1 | 3188 | 1010 | 0.3168 | 874 | 0.2742 | 959 | 0.3008 |
| 0.1 | 3054 | 969 | 0.3173 | 835 | 0.2734 | 920 | 0.3012 |

| | | | | | | | |
|-----|------|------|--------|------|--------|------|--------|
| 0.2 | 2453 | 1653 | 0.6739 | 1761 | 0.7179 | 1876 | 0.7648 |
| 0.2 | 3038 | 2297 | 0.7561 | 2206 | 0.7261 | 2122 | 0.6985 |
| 0.2 | 2756 | 1922 | 0.6974 | 1871 | 0.6789 | 1969 | 0.7144 |
| 0.3 | 2946 | 3131 | 1.0628 | 3137 | 1.0648 | 3109 | 1.0553 |
| 0.3 | 2924 | 2919 | 0.9983 | 2992 | 1.0233 | 3080 | 1.0534 |
| 0.3 | 3289 | 3670 | 1.1158 | 3648 | 1.1092 | 3509 | 1.0669 |
| 0.4 | 2927 | 4818 | 1.6461 | 4650 | 1.5887 | 4580 | 1.5647 |
| 0.4 | 3042 | 4671 | 1.5355 | 4547 | 1.4947 | 4771 | 1.5684 |
| 0.4 | 3274 | 5706 | 1.7428 | 5286 | 1.6145 | 5145 | 1.5715 |

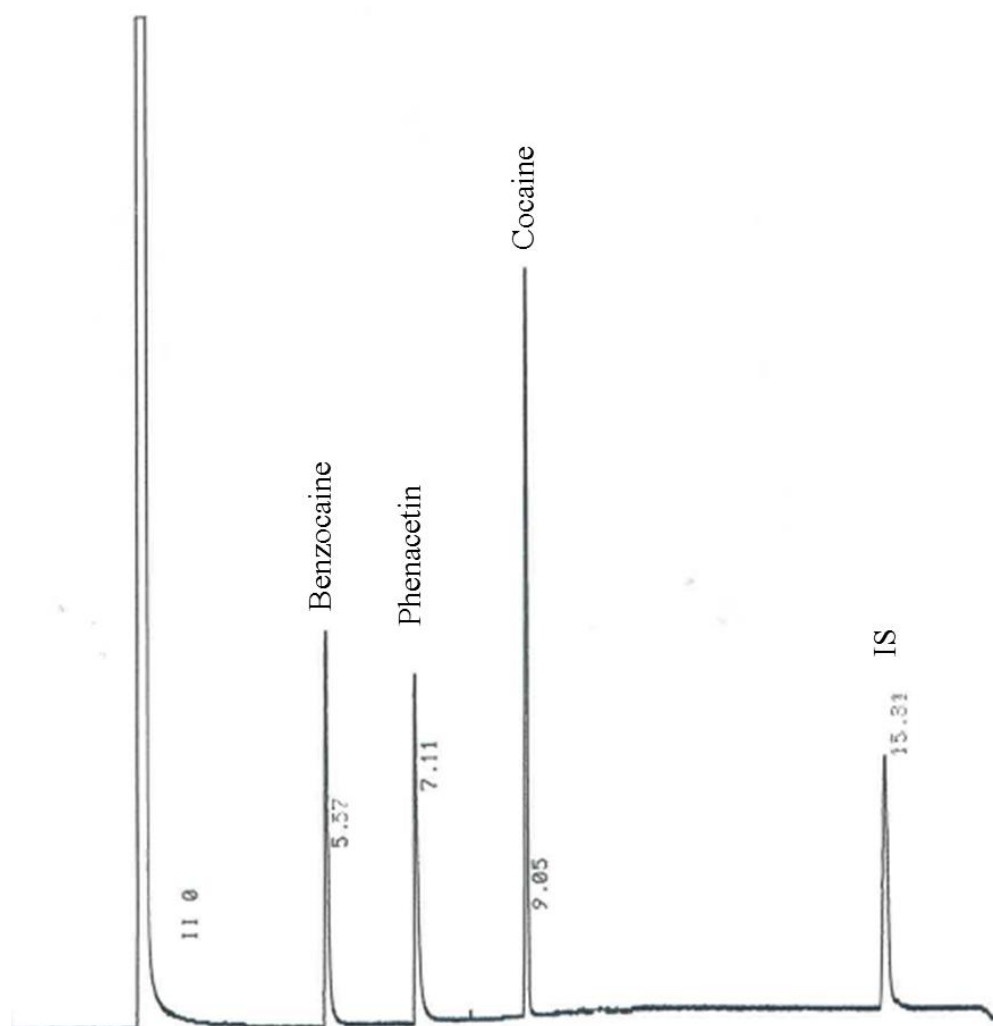


Fig. 4.24. GC-FID chromatogram of a mixture solution of benzocaine, phenacetin, cocaine, and IS.

The reference sample was used to validate the optimised method by weighing six samples (~50 mg) of it and measuring the content of each one separately. The average content of cocaine free-base was 42 % and of phenacetin was 33.6 % (Table 4.15). Comparing with the HPLC method, the reference sample content according to the HPLC method contains 46.0 % cocaine and 34.6 % phenacetin. The differences could be related to the sensitivity of the methods and the solubility of the contents in the solvents used.

The results obtained from different analytical techniques could give information to complete the crack sample profiling and establishing a database to help to identify source cluster of crack samples. Each analytical technique has unique properties which make it more applicable or limited depending on the availability, cost, time and ease and value of information obtained from the analytical test.

Table 4.15

The GC-FID results obtained with six replicates of the crack cocaine reference sample

| sample | weight (mg) | cocaine percentage | phenacetin percentage |
|---------|-------------|--------------------|-----------------------|
| ref 11A | 51 | 41.56 | 33.39 |
| ref 12A | 50.5 | 40.95 | 33.37 |
| ref 13A | 50.4 | 43.84 | 34.21 |
| ref 14A | 50.3 | 42.01 | 33.54 |
| ref 15A | 51 | 41.31 | 33.5 |
| ref 16A | 50.9 | 42.86 | 34.01 |
| average | | 42.08 | 33.67 |
| STDV | | 1.081 | 0.35 |
| RSD | | 2.57 | 1.04 |

Although GC-FID finds wide use in forensic analysis and other profiling procedures, but in this study the aqueous extract layer could not be injected on to the GC column due to the possible content of sugars that may damage/block the column. Moreover, an internal standard is required if this procedure is to be quantitative. Volatilized compounds such as cocaine and phenacetin were sufficiently volatile to be

measured by this procedure without derivatization. If any non-volatile compounds are present, derivatization, usually by silylation, has to be carried out before injecting the solution onto the GC column.

4.4. Conclusions

Profiling samples is an analytical approach that collects nearly complete information about the unknown samples. This approach starts from simple techniques which serve as guide to the next procedure in the chain process to end up with identification and quantification of the contents. Identification results are mainly carried out through qualitative analytical techniques that include: HPTLC, FT-IR, MS, and NMR. The quantitation of results follows from quantitative analysis techniques that include: HPLC and GC-FID.

HPTLC is a time and cost saving analytical technique that provides general information about many components to guide further analysis by comparing the content compounds with expected standards. It can guide into next steps in the case the standards were matched with all or some of the content. However, it does not detect all components such as sugars and the sample is not recovered. Further confirmation for some categories of compounds can be achieved by spray specific reagents to identify the compounds e.g. Dragendorff's reagent which is solution of potassium bismuth iodide ($\text{BiI}_3\cdot\text{K}_4$) used to determine the presence of alkaloids. FT-IR is fast, sensitive, uses a tiny amount of sample; but it gives more complicated spectra in which it is not easy to assign all the peaks or determine the components due to overlapping within the spectrum, the sample is not recovered. FT-IR data could be used for further analysis such as tracking the impurities or sources by PCA, HCA. MS gives the molecular weight of components with a possible formula; but MS is not available everywhere, it needs an expert to run the samples and it is more expensive than other techniques, and the sample is not recovered. NMR analysis is done in a short time, using a few milligrams of sample that can be recovered, and it can be used for qualitative and semi-quantitative analysis. Different NMR experiments such as 2D DOSY can be performed to get information about the structures of the mixtures.

Chapter 5

Multivariate statistical analysis of ^1H NMR data of street crack samples

5.1. Introduction

Cocaine is available in two chemical forms: cocaine hydrochloride and cocaine free base “crack”. Each cocaine form is administered in different administration routes such as snorting for salt and smoking or injecting for the free base form, the purity range 1-90% for street samples [73]. Cocaine is a natural alkaloid which is purified from the natural source, while the purified product will contain other minor natural compounds. The amount of those compounds depends on the environmental conditions and the cultivar. Detection of the content of the cocaine and other associated minor natural alkaloids was used as a fingerprint for the seized samples to identify the geographical origin of the samples [74]. Moreover, crack cocaine and cocaine hydrochloride samples contain cutting agents either adulterant substances (pharmacologically active) or diluents (pharmacologically inert).

The differences between the purity and adulterants in different studies relate to the market circumstances and the availability of cutting agents in each area. So these differences could be used to track the distribution networks and the origin of the seized drug samples by applying certain statistical techniques [75]. Statistical techniques that were used in drug classification are Principal Components Analysis (PCA), and hierarchical cluster analysis (HCA) on the analytical results [76].

PCA is a multivariate statistical analysis that aims: to decrease the number of variables; to isolate the unrelated variables; to improve the data to achieve desirable objectives; and to simplify data for further analysis [77]. PCA is one of the essential chemometric methods. The collected data of analysed samples are reduced to principal components by PCA. The first component accounts for most of the variance between the samples, and subsequent components account for progressively less variance. The numbers of principal components are much less than the number of variables (spectral shifts); the most part of the data set is represented by few components that describe the whole chemical shifts variables in the data set [78].

Each principal component can be described by a specific “loading” for each of the original variables. Each sample is described by a “score” for each principal

component. In this thesis, for a principal component, the loading vector is a spectrum while the sample's score is the amount of specific loading in that sample. The loadings in each principal component represent certain segments of the spectra which indicate the principal differences between samples. Comparatively, the scores supply information about the extent to which the information described by the loading data are low or high in analysed samples. Thus, the scores could be recognised as concentrations of multivariate variables [78]. Scatter plots can be used to plot scores against each other to provide a map of all samples in score plot. Samples will be clustered in a score plot depending on similarities of their spectra between principal components. This means of grouping samples and then discovering the model of clustering the samples by identifying the principal components is recognised as one of the strengths of PCA. Winning and co-authors showed the application of PCA and another multivariate technique to use NMR data to supply an extensive overview of complicated NMR data with many variables [78].

Hierarchical cluster analysis (HCA) is considered as one of unsupervised recognition algorithmic model, where different samples (objects) from the set of data are clustered together depending on their similarities. The distances of samples measure the similarities between samples in the data set. In the HCA, dendrogram shows the samples and the distance between samples. At the bottom of the dendrogram, samples are displayed individually; similar samples are linked via horizontal lines. However, a new cluster is established by linking two or more linked clusters. Similar clusters are linked at low level of distance, while dissimilar clusters are linked at high level [79].

HCA and PCA use the data of NMR spectra after conversion into numeric sets of data. The purpose of the PCA, HCA and other statistical techniques is to find out whether the samples are similar or not. Previous attempts to identify the geographical origin of drugs by natural minor components that differentiate between samples used Raman spectroscopy or GC-MS [35]. Esseiva applied PCA and correlation calculation to classify drug samples using results of chromatography [80]. In Sanchez's study, NMR data of seized crack cocaine samples were used to find out the relation between the samples through the similarity between them [81]. This could give information about the source of the samples and the distribution route of the drugs. All of this may facilitate the police in tracking the sources and prevent more drugs being sold.

The health problems for users are not only caused by drugs, but also caused by the cutting agents which may be added to increase bulk, to get similar properties of the drug, and to improve the drug properties [82, 83].

In this study, chemometric treatment is used to achieve the aim of extracting information from the NMR data. PCA and HCA are applied on the NMR spectra of the samples to identify the relation and cluster models. A combination of the two statistical techniques (PCA and HCA) will enable potential linkages to be made between crack samples seized at different times in Swindon, UK to indicate a similar origin or channel of distribution. This can be combined with detection information to get improved investigation strategies.

5.2. Results and Discussion

5.2.1. Protocol A

PCA was applied to the NMR spectroscopic data obtained from analysing the deuteriated chloroform layer content only for 34 crack samples. The scree plot is shown in Fig. 5.1. The results show that there is a main cluster (28 out of 34 components) because most of the samples contain the same compounds.

Fig. 5.2 shows that cocaine base, phenacetin, and benzocaine had a low score for PC1 which refers to the mixture of cocaine and phenacetin, while cocaine had a high loading for PC2 only compared with other two standards. The samples containing benzocaine had low loading for two components (PC1, PC2), while there is gradual distribution for other crack samples that have cocaine and phenacetin at different percentages. The dendrogram of the HCA results of 34 crack samples showed how the pure phenacetin, pure benzocaine and two samples containing benzocaine were separated from the main cluster that contained samples containing a mixture of cocaine and phenacetin. All of these samples have low scores according to PC1 and PC2. The cocaine pure and sample and other three samples that are main cocaine had low score as well according to PC1, but they had high scores according to PC2. All of these two mini clusters were separated at the bottom of the dendrogram with different relation to the main cluster depending to the similarities of each one (Fig. 5.3).

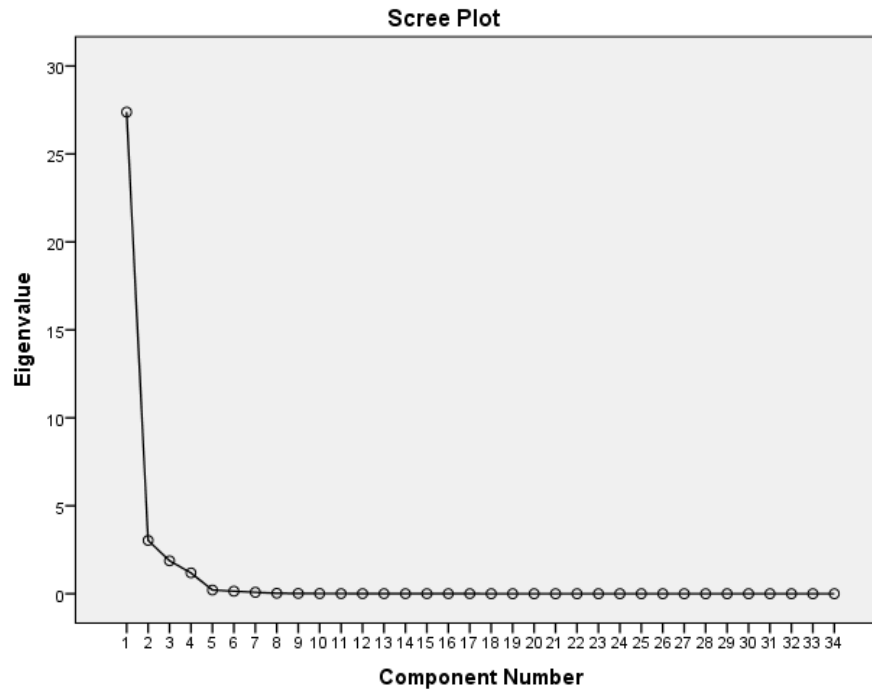


Fig. 5.1. The Scree plot of PCA results by protocol A.

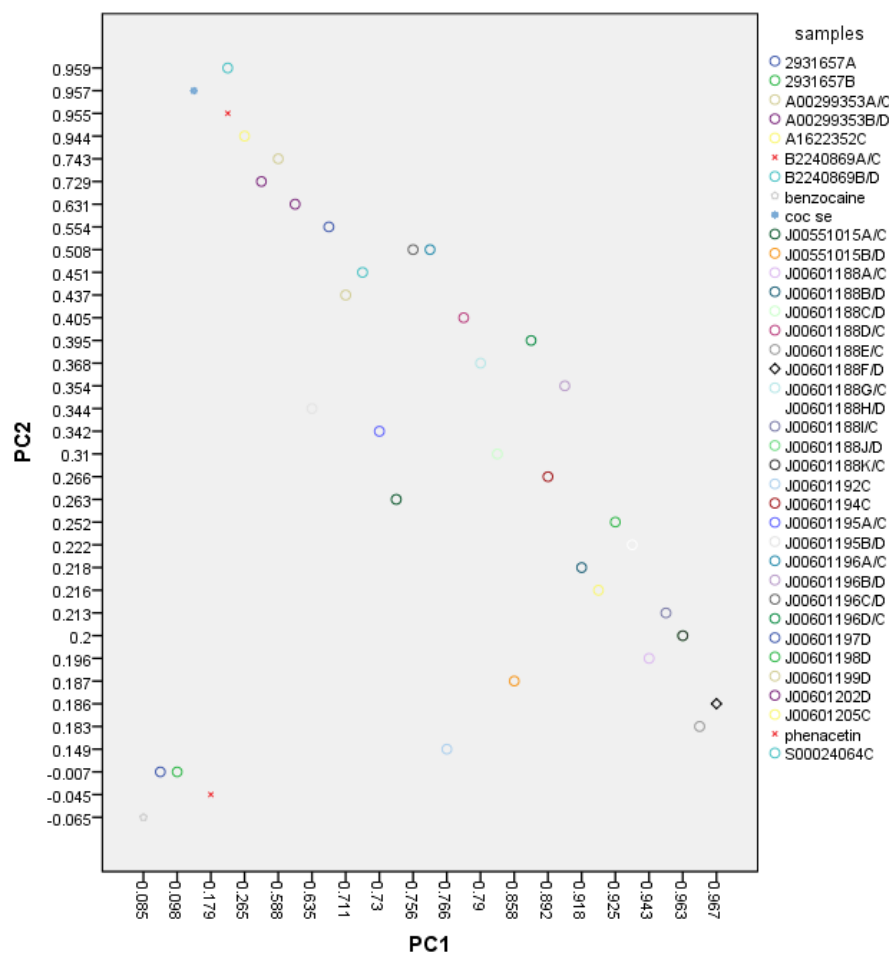


Fig 5.2. PCA scores plot of the first two PCs.

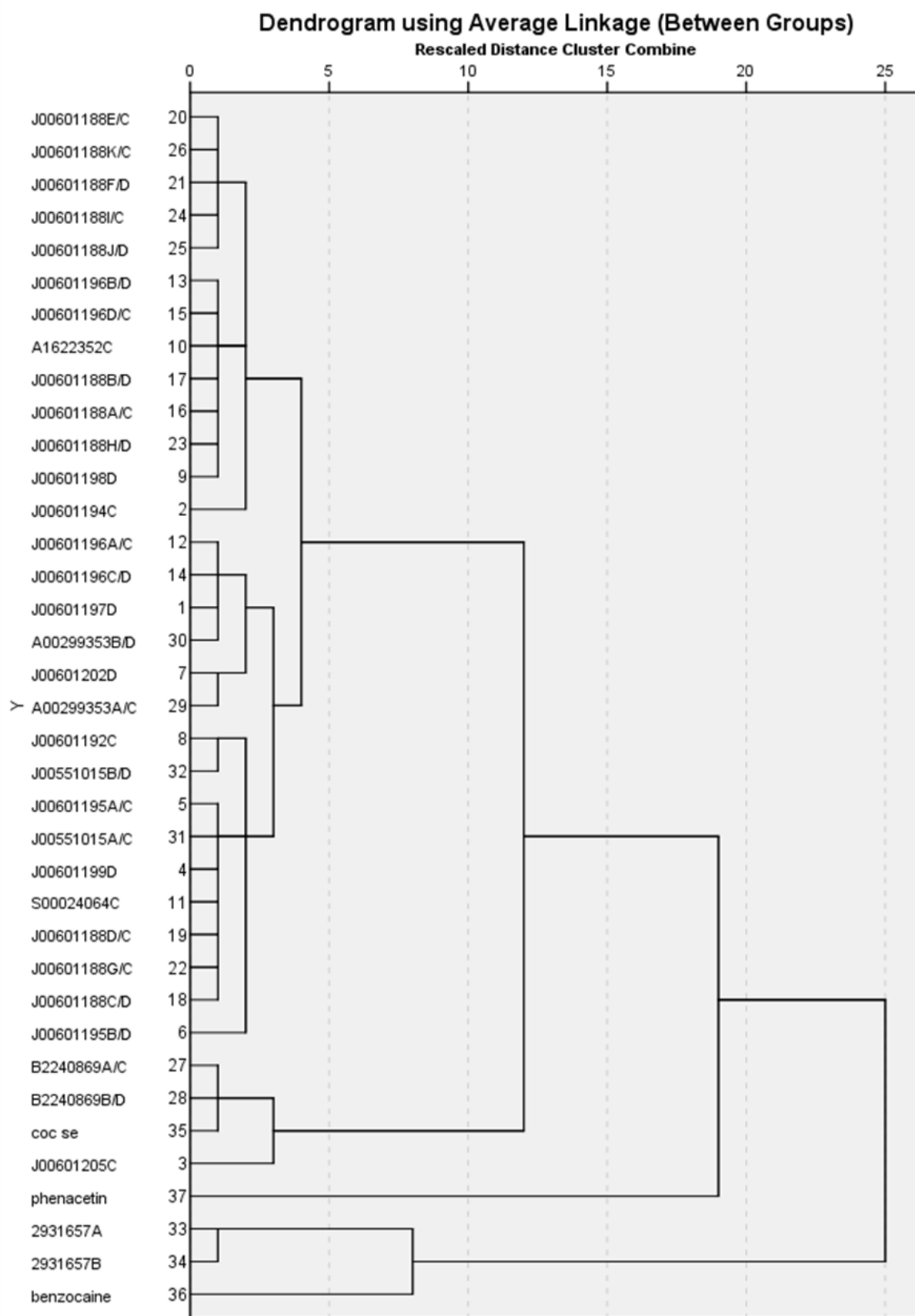


Fig. 5.3. Dendrogram using average linkage between samples obtained by HCA
(Protocol A)

5.2.2. Protocol B

This pattern of mainly one cluster could be caused by the partition step of protocol A, which removed aqueous components to the D₂O layer. Thus, protocol B was employed to analyse the whole content of the samples together to differentiate as much as possible between the samples. This was carried out using another series of seized samples.

¹H NMR spectra of 112 crack samples and standards of common adulterants were analysed by the statistical techniques (PCA and HCA) to probe for more information. The scree plot is shown in Fig. 5.4. The results show that there is one main cluster and a few minor clusters.

HCA presents the outcome through a dendrogram chart according to the variance weighted distance between cluster centres (Fig. 5.5). It gives an indication about nearby clusters and the level of variance distance between samples. There are two sets of sample clusters next to each other that have low variance compared with the more distant cluster. These two sets (Cluster 1A, 1B) include 78 samples (32, 46 samples respectively) out of 112 samples. There are three sub clusters (Cluster 2A, 2B, 2C) which look similar and come together next to cluster 1, and form the second cluster. They include 25 samples (5, 13, 7 samples respectively).



Fig. 5.4. The Scree plot of PCA results by protocol B.

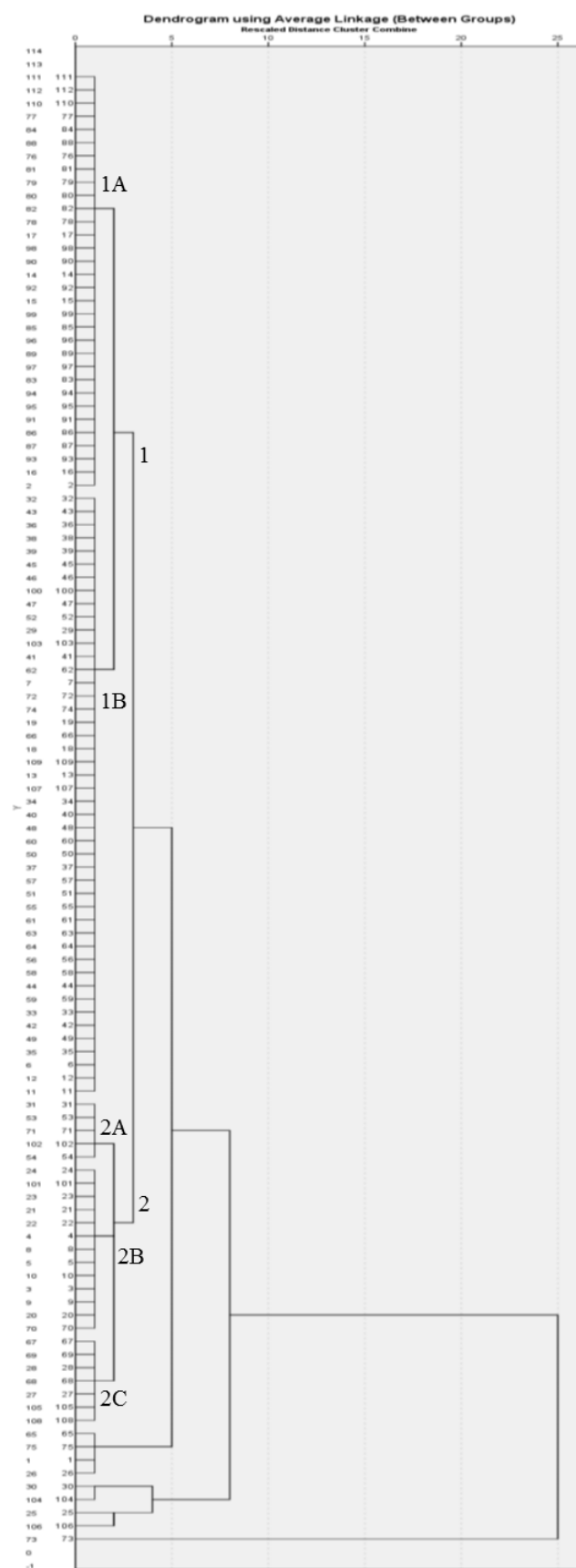


Fig. 5.5. Dendrogram using average linkage between samples obtained by HCA (Protocol B).

NMR spectra from the clusters 1A and 1B show that the samples contain cocaine base and phenacetin with different percentages (Fig. 5.6). Visual comparison alone gives no clear explanation for the splitting of the samples into two sets compared. This difference could be due to minor compounds which exist naturally with cocaine, different impurities in the phenacetin, different preparation procedures, and residue of solvents or by-products of preparation methods.

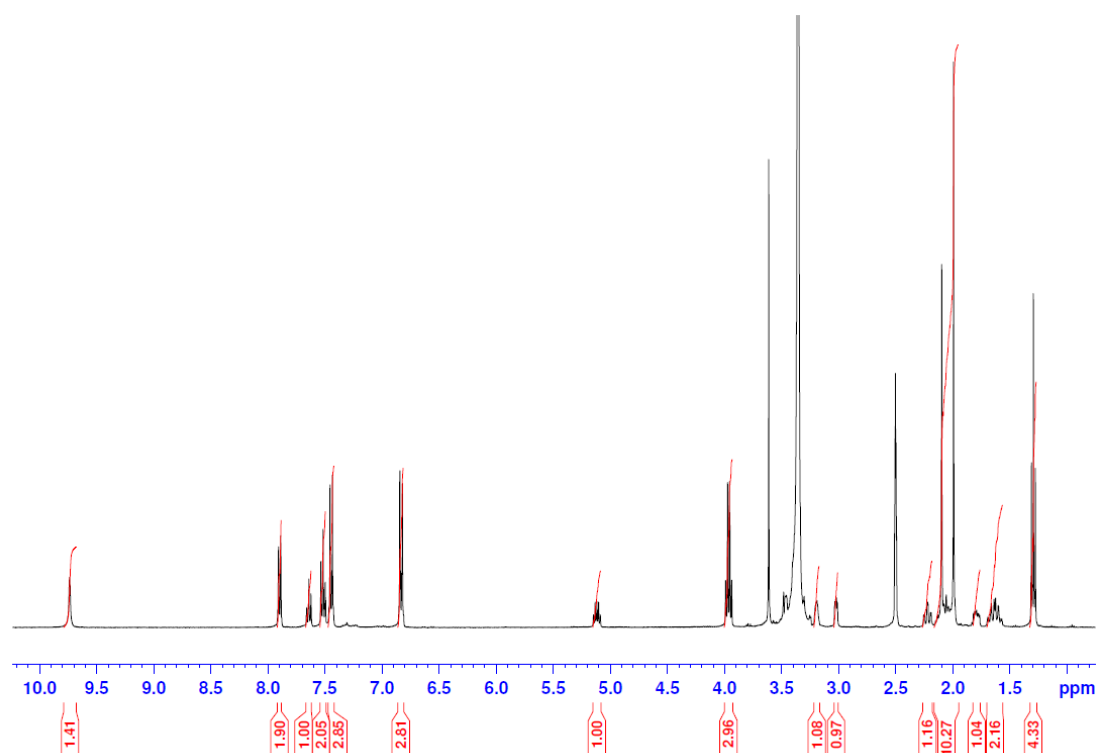


Fig. 5.6. NMR spectrum cocaine and phenacetin crack sample
(Representing PC1A & PC1B).

Cluster 2A which consists of five samples contain mainly cocaine free base. Fig. 5.7 is an NMR spectrum from one sample, highly pure drug without adulterants compared with samples in the previous cluster. At the bottom of the dendrogram in Fig. 5.5, a single sample (sample 73) separates out from the other clusters. The link between this sample and the other samples is very weak, and the NMR spectrum of this sample (Fig. 5.8) is negative for the presence of cocaine and any other identified adulterants in other samples.

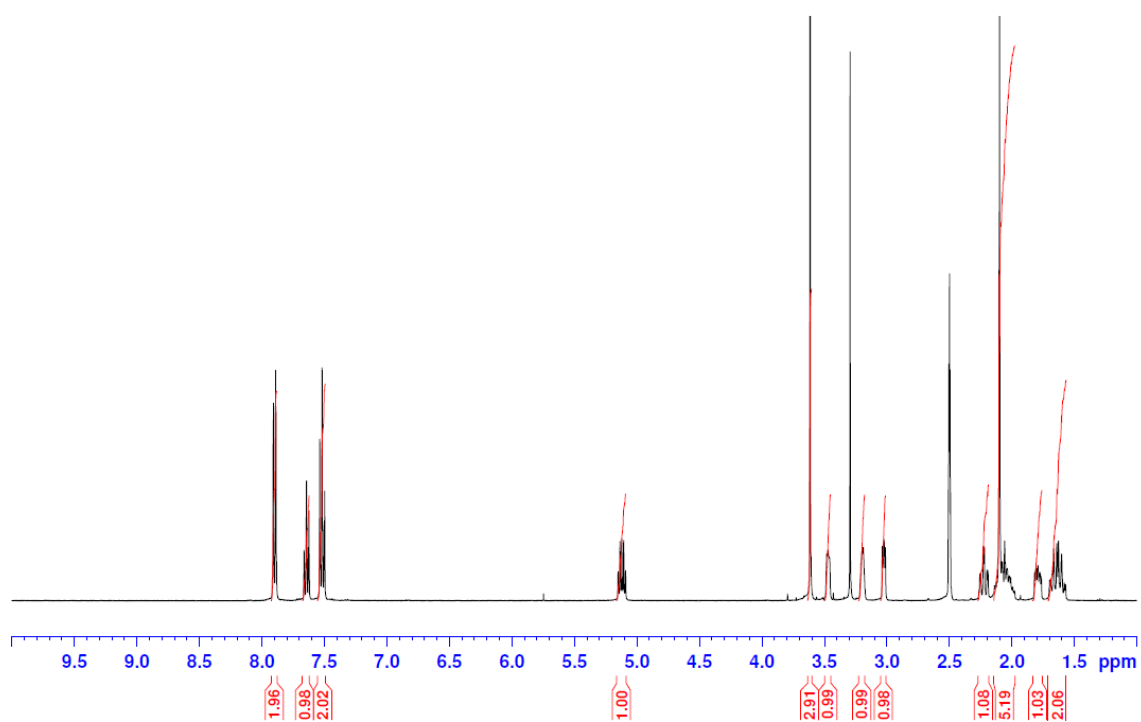


Fig. 5.7. NMR spectrum for crack samples mainly cocaine free base (Representing PC2A).

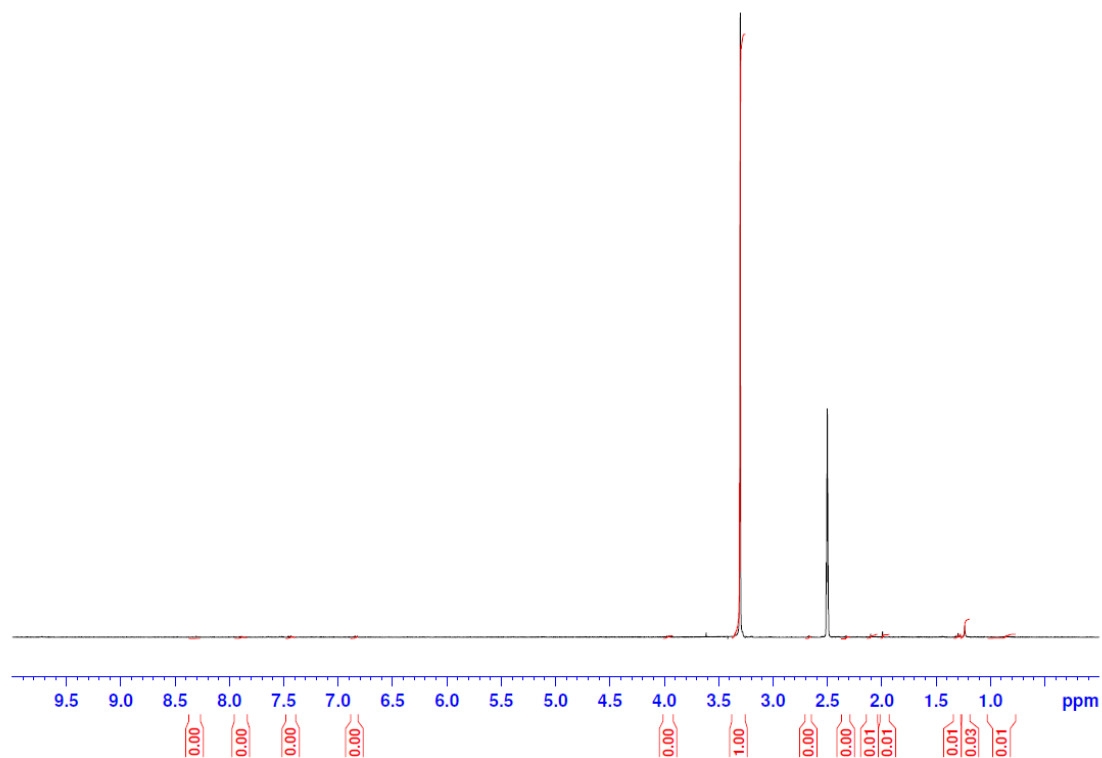


Fig. 5.8. NMR spectrum of sample J00601201 (code 73).

The same NMR spectral data were analysed by PCA to attempt to understand the dendrogram pattern and to determine the extent of agreement between the two statistical approaches.

PCA showed that the total variance within this series of samples could be largely accounted for by four principal components. The matrix of the components (Fig. 5.9) shows the relation between them and how samples are gathered to form few components.

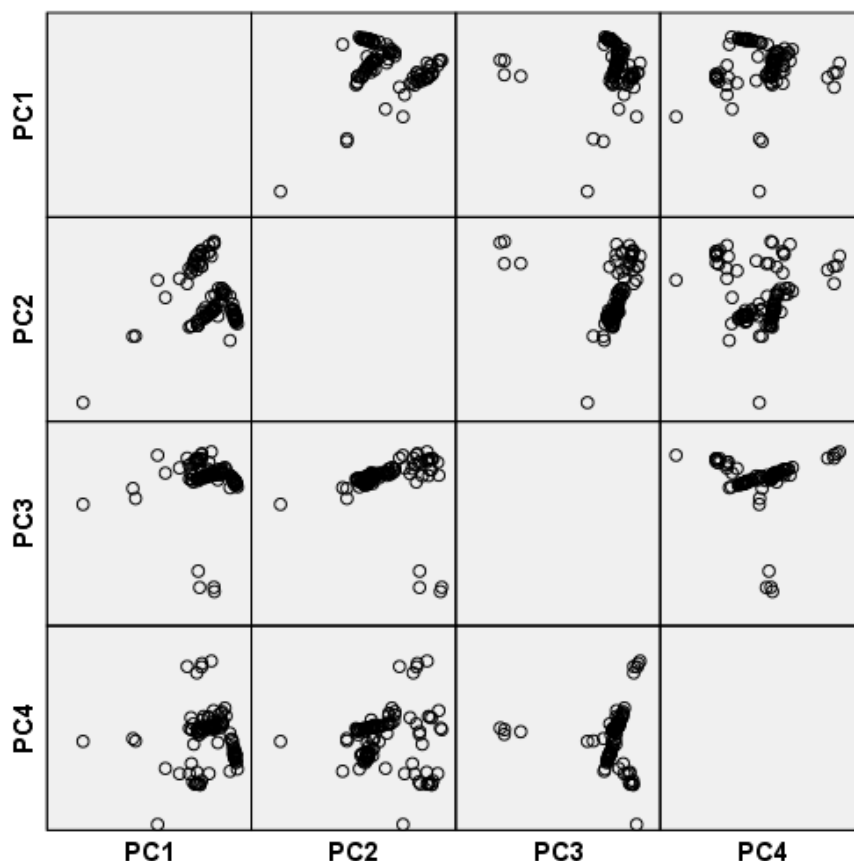


Fig. 5.9. Matrix of four principal components.

Fig. 5.10 distributed the samples apparently into two clusters plus outliers. Fig. 5.10 gives details that agree with the dendrogram (Fig. 5.5) where PC1 (61.6 % of variance) matches with cluster 1 in the dendrogram where both contain the same samples. Those samples contain cocaine base as drug and phenacetin as adulterant from the NMR spectra, but there is now further information why they are separated into two subclusters by using this NMR data analysis. Also, PC2 (17.5 % of variance) which contains in this case a group of samples which match with that cluster 2 in the

dendrogram, where cluster 2 is formed by gathering three subgroups which may indicate that PC2 is the same and it is formed by subcomponents.

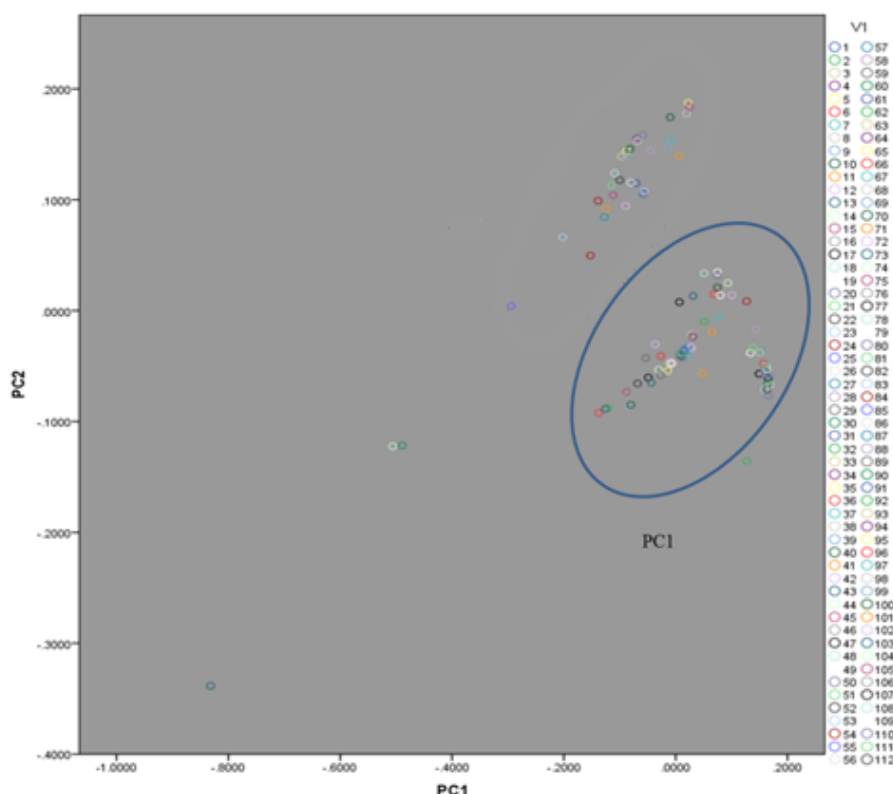


Fig. 5.10. PCA scores plot with PC1 highlighted.

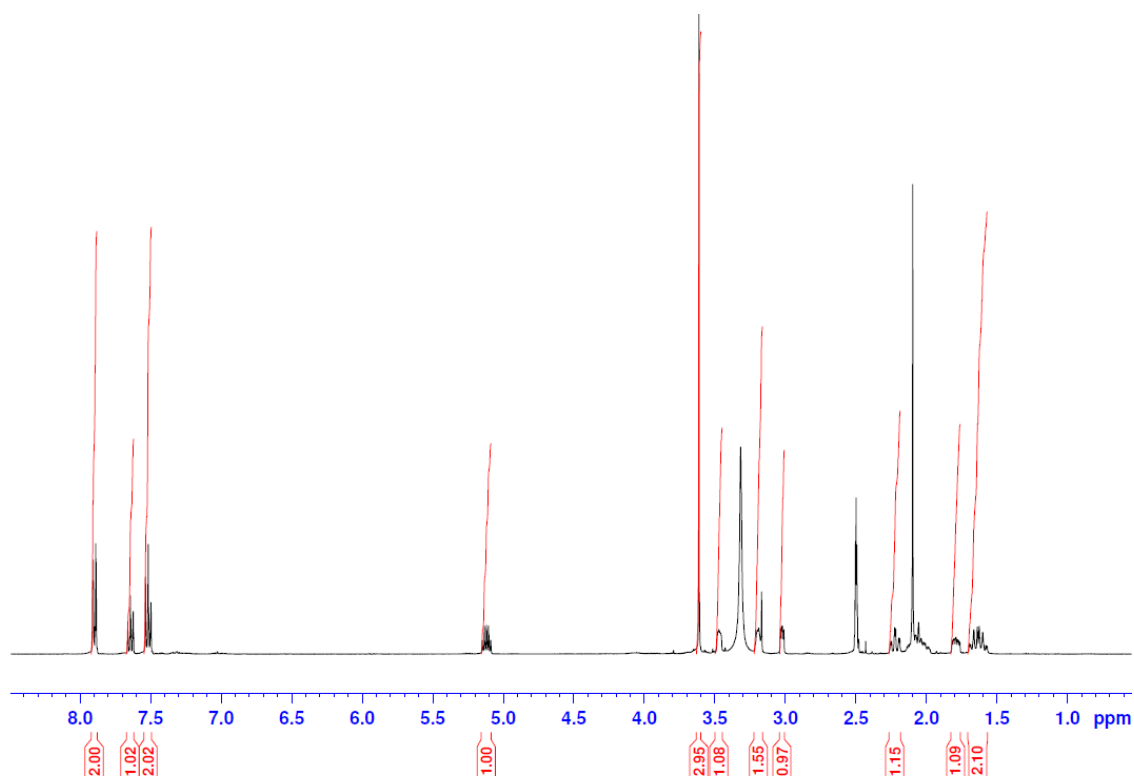
The centre samples (Table 5.1) of sub groups of cluster 2A, 2B, 2C (102, 4, and 68) are located in PC2 at different locations. The content of those samples (102, 4, and 68) was identified by their NMR spectra (Fig. 5.11), and shown to be different because sample 102 contains cocaine (almost pure), sample 68 contains cocaine and another cutting agent and sample 4 contents are unknown. Thus, PC2 appears to represent samples that do not contain cocaine and phenacetin together as a mixture.

Table 5.1

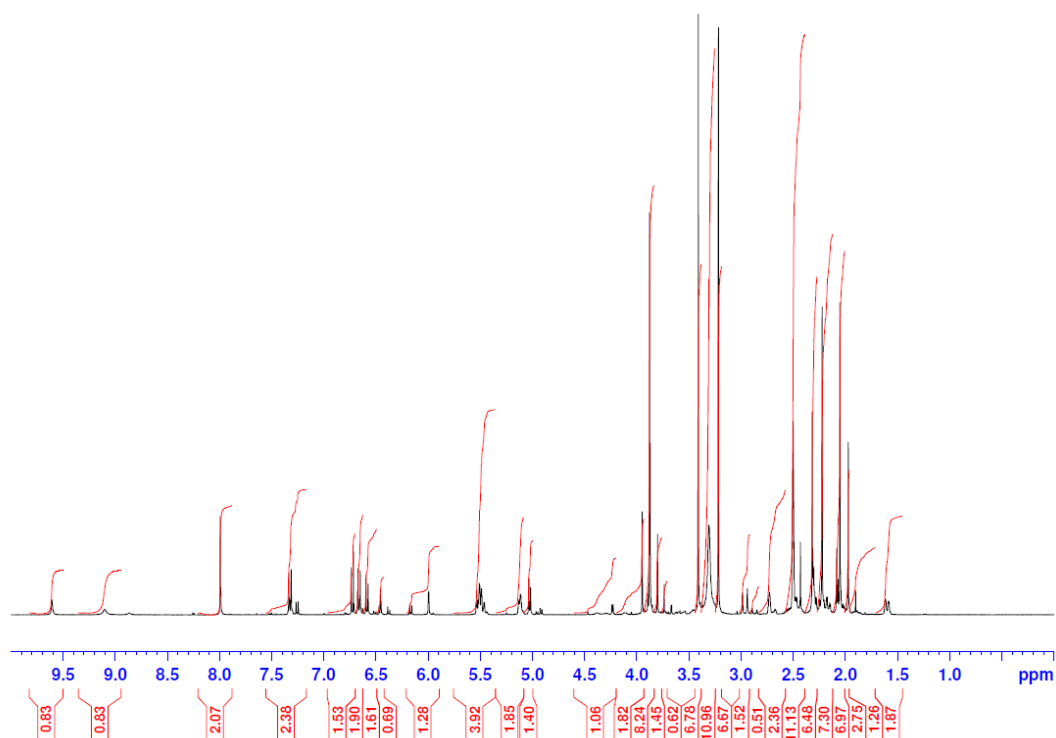
Central samples in cluster 2 details

| Sample number | Code | Sample name |
|---------------|----------|-------------|
| 102 | Mzs12849 | JG600323-2 |
| 4 | Mzs11931 | F263408-4-b |
| 68 | Mzs8846 | J00601203 |

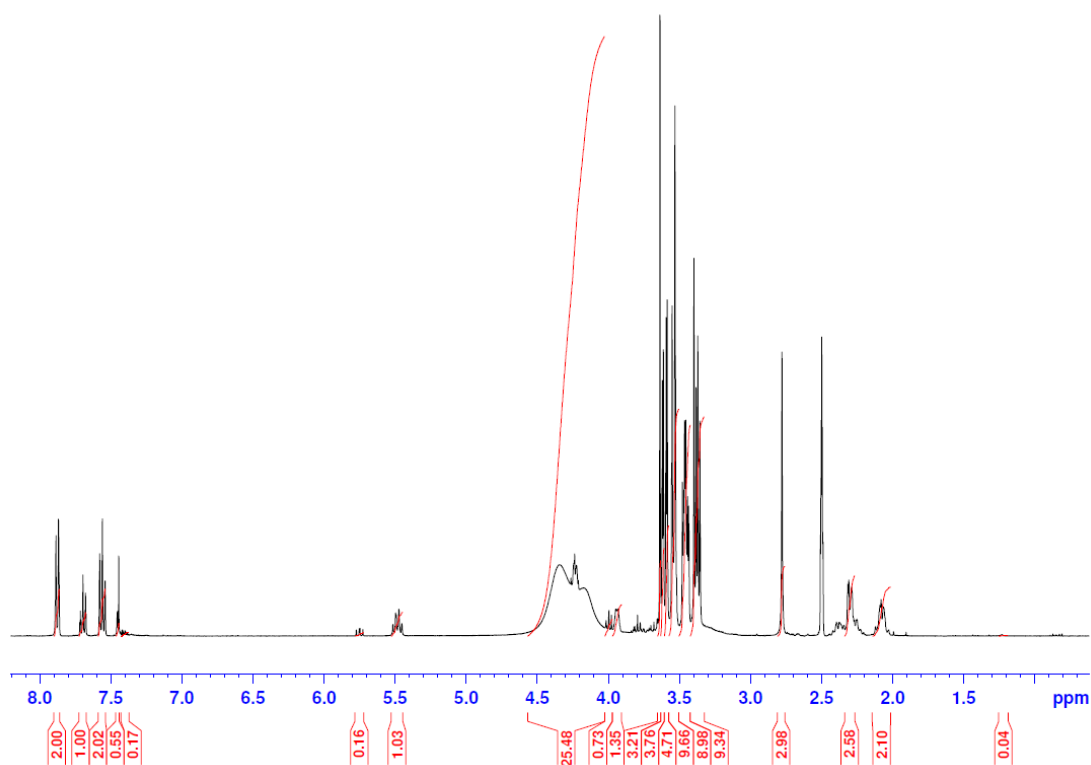
Plots of PC3 against other components (Fig. 5.12) that show the principal component 3(PC3) (5.4 % of variance) resolves a few samples that are separated from other samples with negative loading (-0.3000) compared with the others. This component matches cluster 3 in the dendrogram which has 4 samples (1, 65, 75, and 26) (Table 5.2), they are either benzocaine as sample 1, or samples which include mainly benzocaine and cocaine.



a. NMR spectrum for sample JG600323-2 (code 102) (Representing PC2A)



b. NMR spectrum for sample F263408-4-b (code 4) (Representing PC2B)



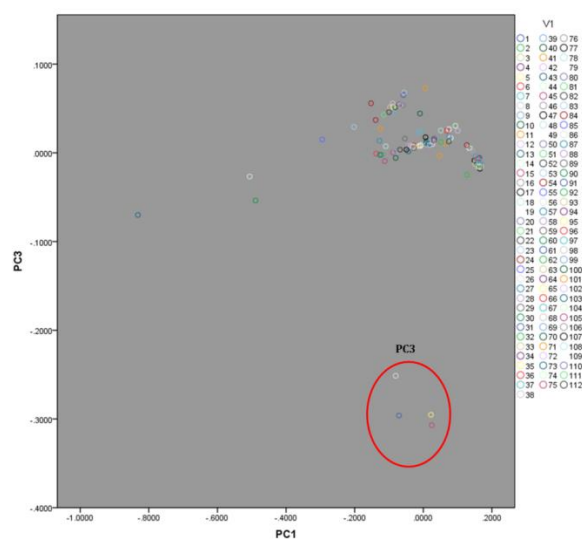
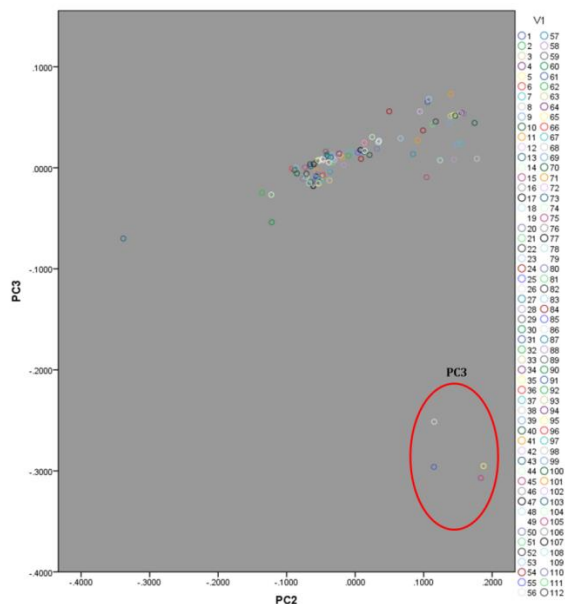
c. NMR spectrum for sample J00601203 (code 68) (Representing PC2C)

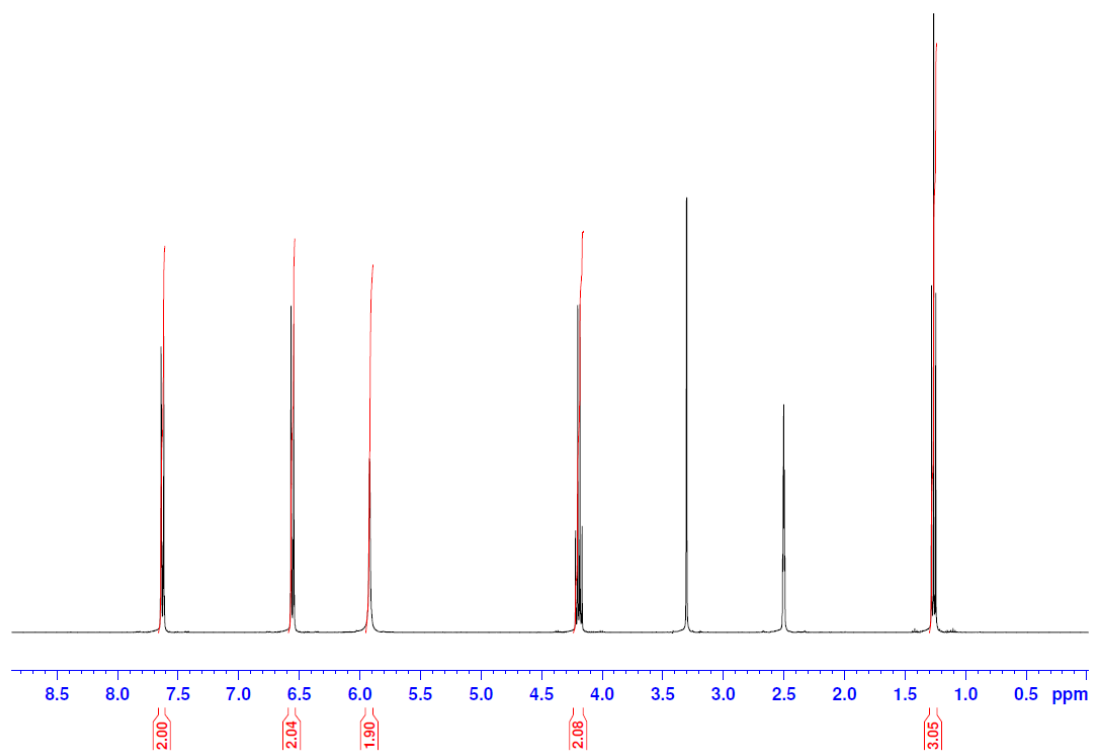
Fig. 5.11. NMR spectra for samples (a. 102, b. 4, and c. 68) respectively.

Table 5.2

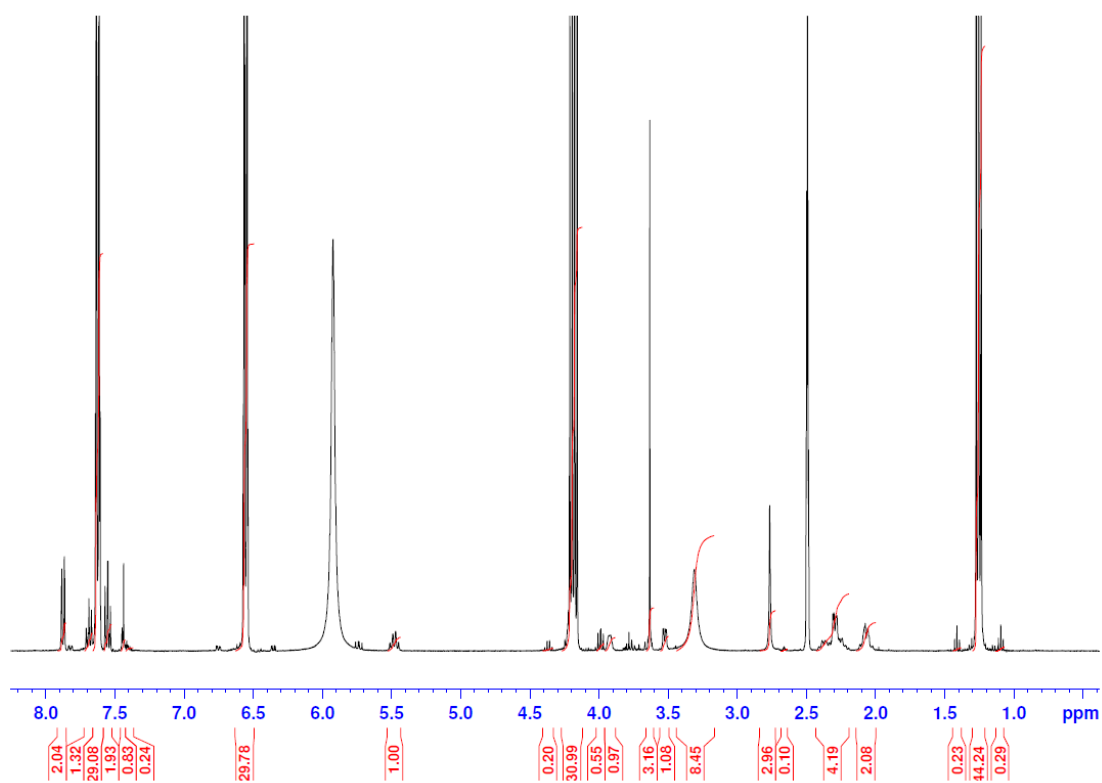
Details of cluster 3 samples

| Sample number | Code | Sample name |
|---------------|----------|-------------|
| 1 | Mzs11891 | Benzocaine |
| 65 | Mzs8843 | J00601187 |
| 75 | Mzs8874 | 2931657C |

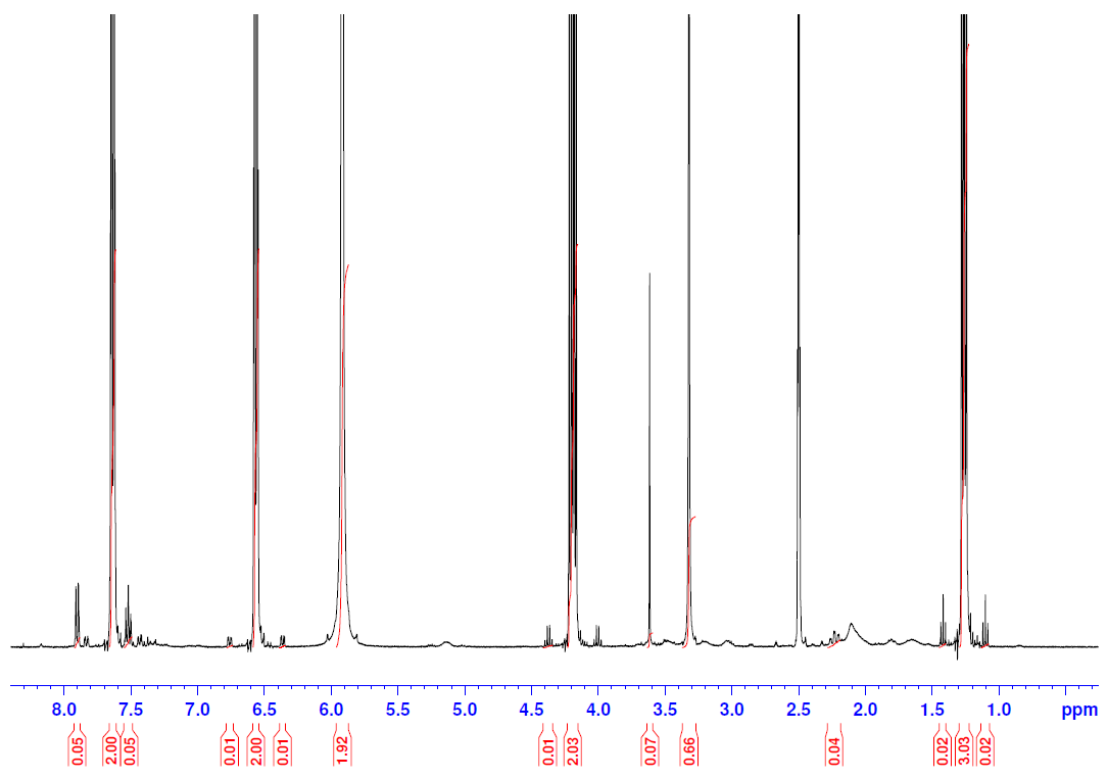
**Fig. 5.12.a.** PCA scores plot with PC3 highlighted.**Fig. 5.12.b.** PCA scores plot with PC3 highlighted.



a. NMR spectrum for benzocaine sample



b. NMR spectrum for sample J00601187



c. NMR spectrum for sample 2931657C

Fig. 5.13. NMR spectra for PC3 samples.

NMR spectra (Fig. 5.13) provide evidence for the content of those samples respectively. PC4 includes five samples (4.5 % of variance) (Table 5.3). The NMR spectra of those samples (Fig. 5.14) show that they contain mainly cocaine base. So this principal component resolves cocaine base standard and mainly pure samples.

Table 5.3

Details of principal component four (PC4)

| Sample number | Code | Sample name |
|---------------|----------|--------------|
| 31 | Mzs10332 | J 00601205a |
| 53 | Mzs10904 | F 263408–2gg |
| 71 | Mzs8870 | J0060120b5b |
| 102 | Mzs12849 | JG600323–2 |
| 54 | Mzs10983 | JSC |

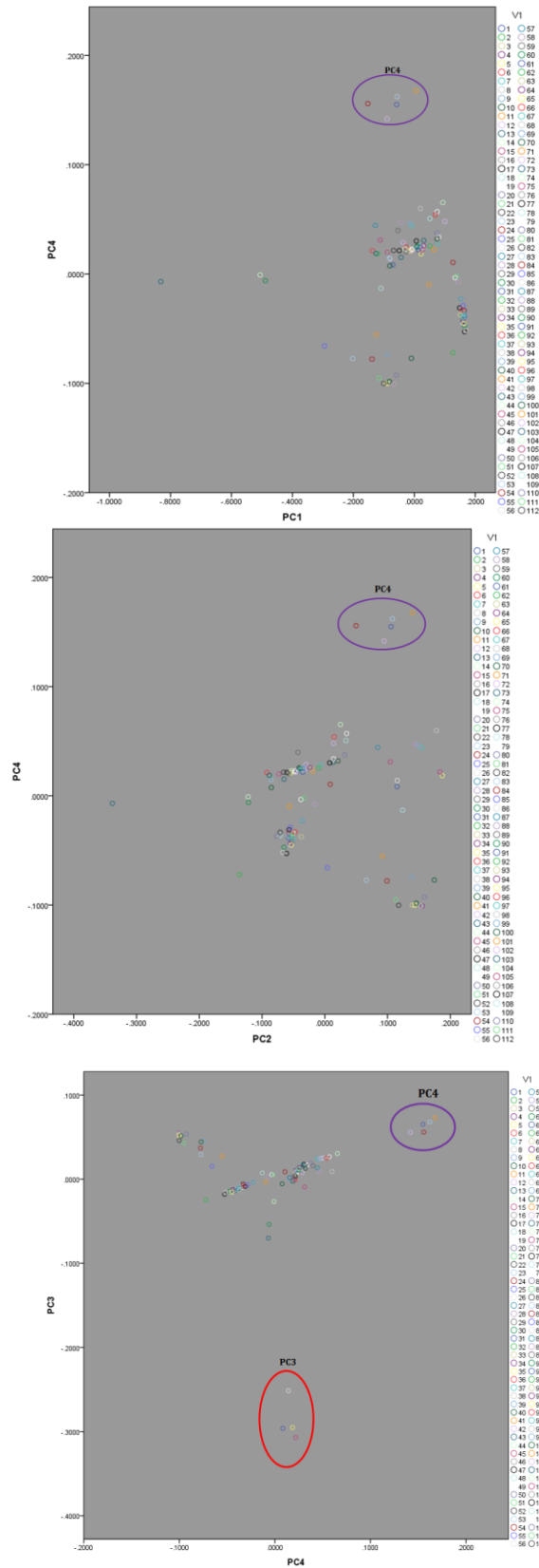
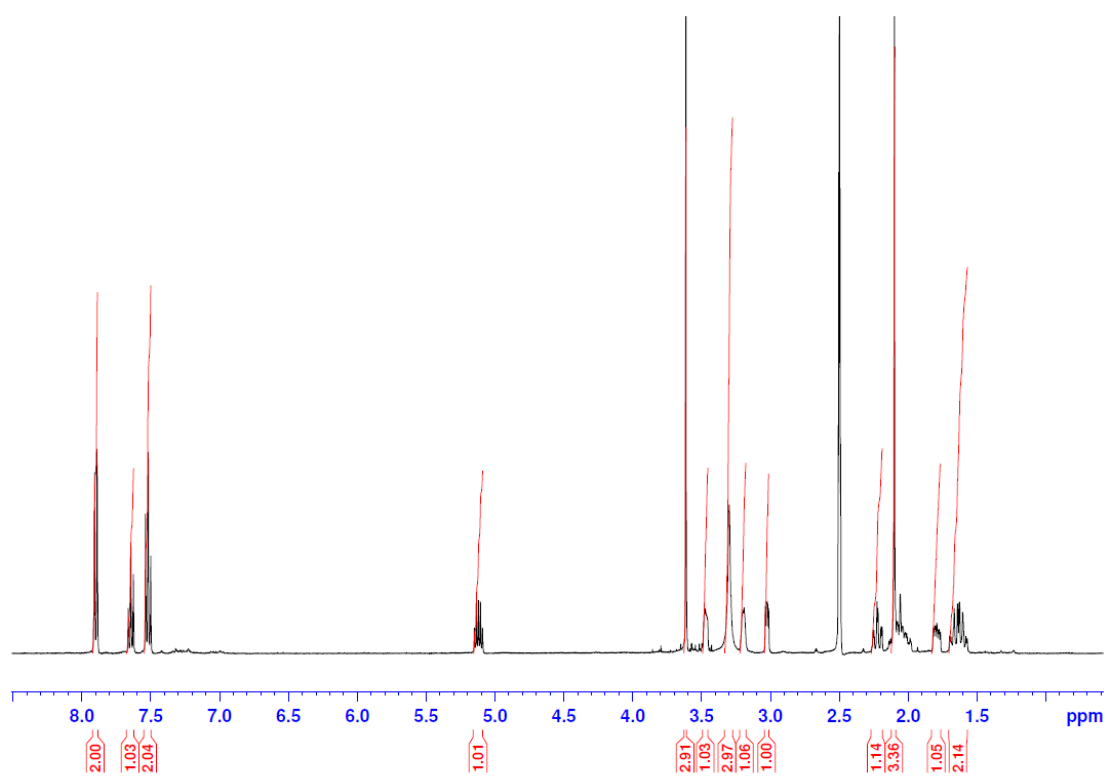
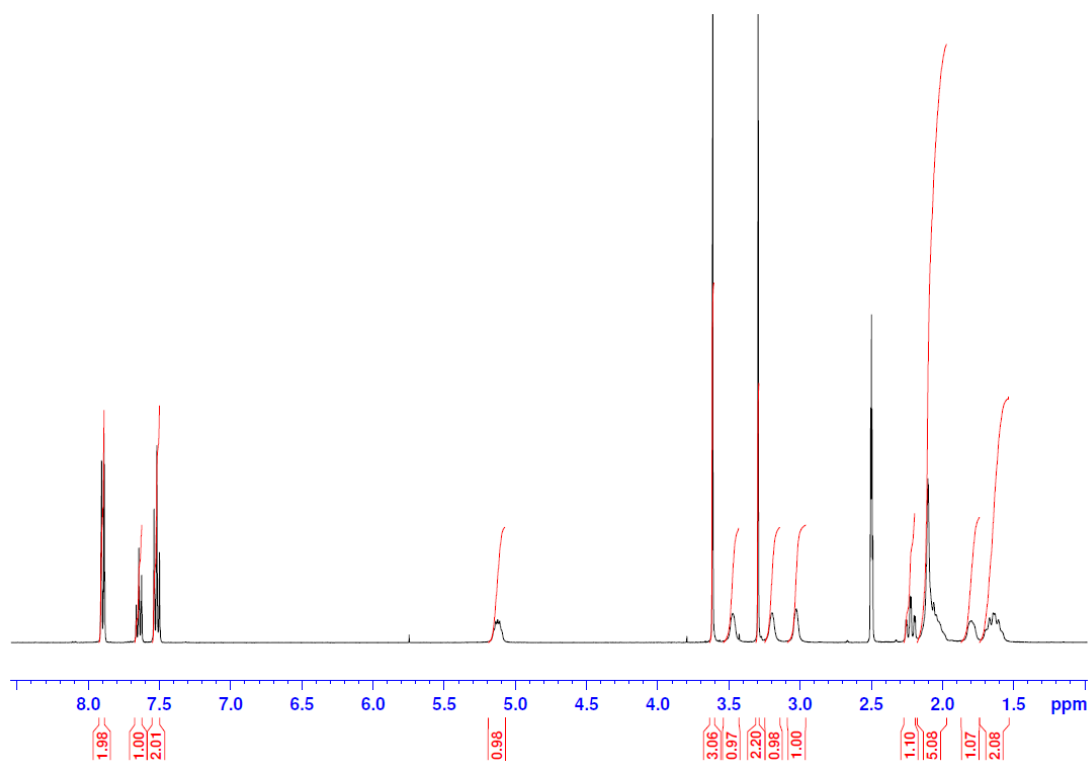


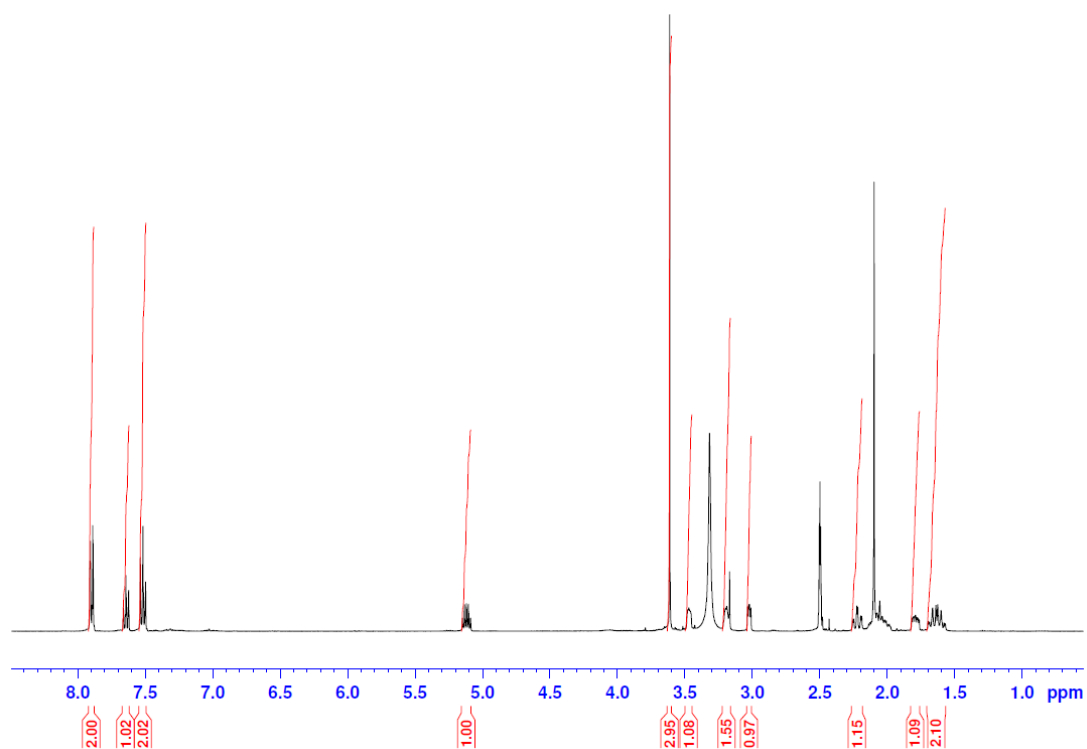
Fig. 5.14. PCA scores plot with PC4 highlighted.



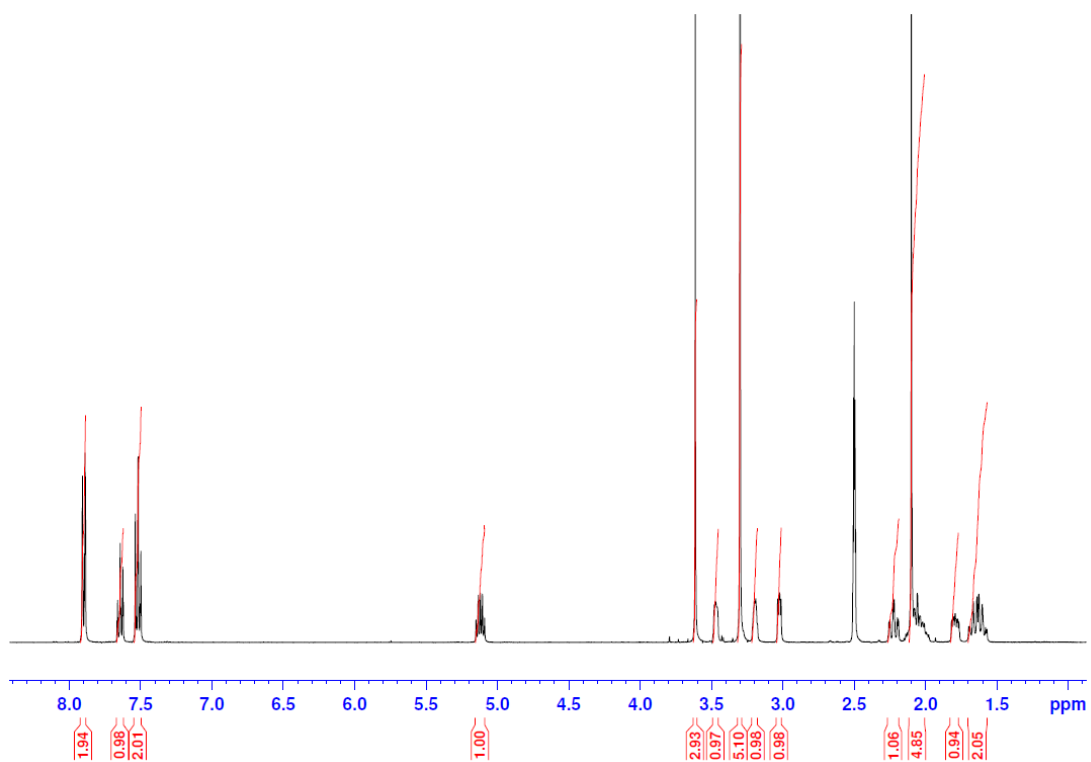
a. NMR spectrum for sample J 00601205



b. NMR spectrum for sample JSA (pure cocaine free-base prepared by the ammonia method)



c. NMR spectrum for sample JG 600323-2



d. NMR spectrum for sample JSC (pure cocaine base prepared by the bicarbonate method)

Fig. 5.15. NMR spectra for samples of PC4.

Two of the samples within this cluster, JSA and JSC were samples of pure cocaine base, prepared in this laboratory from the same sample of pharmaceutical grade cocaine HCl using ammonia and sodium bicarbonate respectively to convert cocaine HCl into cocaine base. They are not identical on the plots in the PCA results and thus more samples and preparations could provide information regarding the residues of preparation materials in the analysed final product.

Results of PCA analysis could also be presented as 3D plots. 3D plots can be used to explain the content of some components, e.g. PC2 which is an accumulation of samples that do not contain the mixture of cocaine and phenacetin. In Fig. 5.10, most of the samples gathered apparently together in two components (PC1, PC2) without any details about PC3 and PC4, while in Fig. 5.16, the samples of PC3 were separated because they had different mixtures to PC1. Similarly, PC4 resolved a small cluster of samples in the 3D plot in Fig 5.17. The results of relationships between principal components explained by 3D plots (Figs. 5.16, 5.17, 5.18) agreed with the HCA dendrogram (Fig. 5.5). The dendrogram showed different levels of links between the samples or clusters which reflect the various levels of similarities, and at the same time the 3D plots of PCA presented the components at dissimilar levels of proximity to each other depending on the loading scores which represented the similarity between the samples and the principal components.

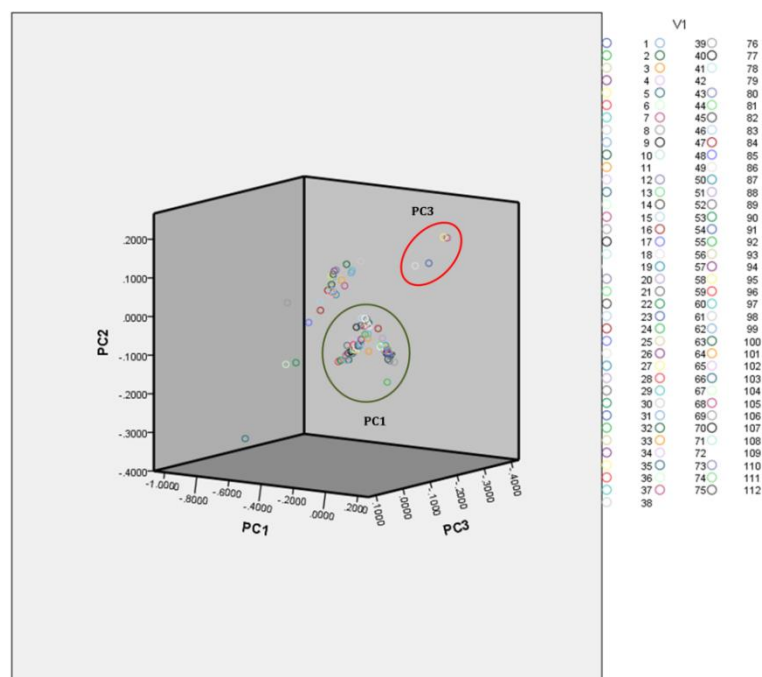


Fig. 5.16. PCA scores plot of PC1 and PC3.

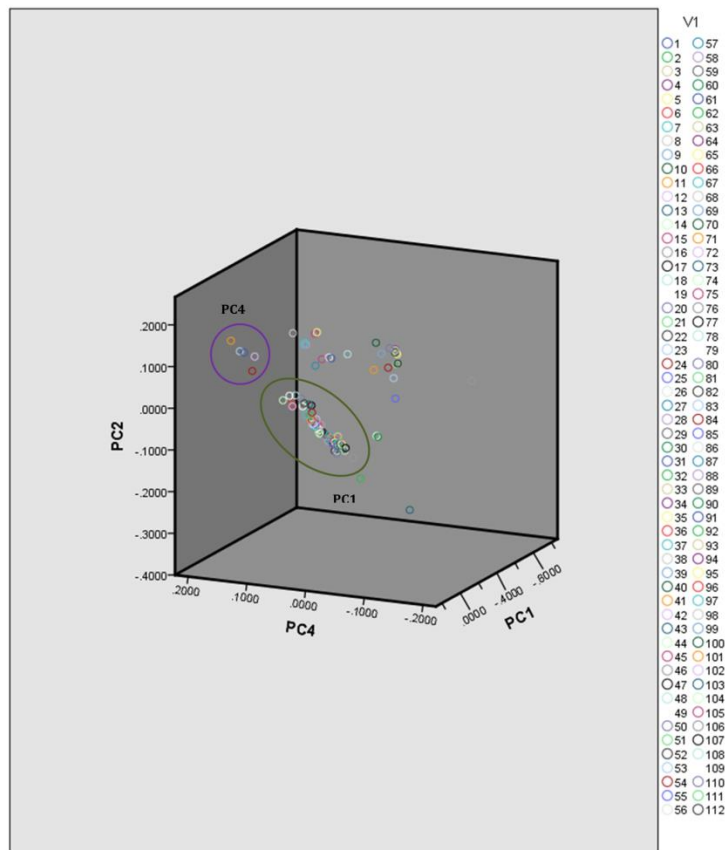


Fig. 5.17. PCA scores plot of PC1 and PC4.

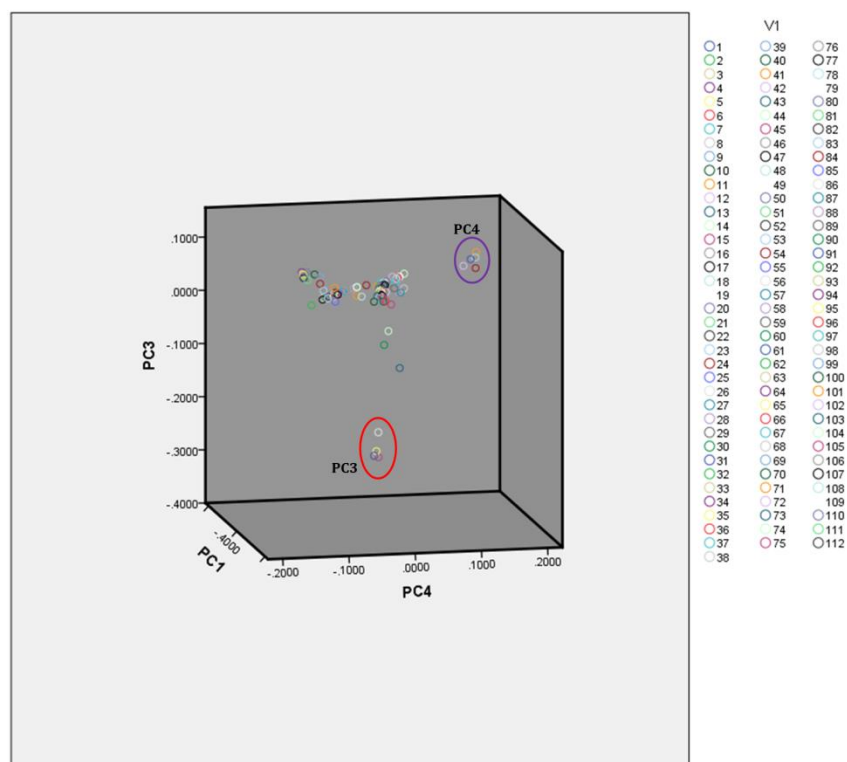


Fig. 5.18. PCA scores plot of PC3 and PC4.

5.3. Conclusions

NMR spectroscopy was used to identify the content of seized crack samples as one of profiling procedures. The role of the outcome of PCA and HCA results based on NMR data is to define any link between the samples, improve the investigation results, and develop techniques for tracking across the drug market. The analysed samples clustered in one main cluster contained cocaine base and phenacetin, and three smaller clusters contained benzocaine as cutting agent or the samples were mainly cocaine pure. Many factors are involved in the continuously changing drug market. Also, this technique could be used as harm reduction message to show the differences between cocaine samples and crack samples depending on their content and the health problems could be linked to each cluster as results of cutting agents effects.

So, updating the profiling and classification techniques is required to look for any linkage between samples from different places and at different times. The combination of analytical and statistical techniques showed the ability of clustering the samples depending on their content. In this study, the seized street samples were clustered into four principal components.

The results presented in this study reveal that the applied analysis can help evidentially and provide some intelligence to the police and forensic investigators. These results and this approach can help to establish a database that tracks the trafficking and distribution channels of different seized samples that were provided from various locations at different times. The same source of samples and the sensitivity of technique used were the advantages of the applied approach.

Furthermore, more variables could be used for the same aims such as characterization of minor components besides the adulterants, analysing more samples from different locations, and using other analytical techniques and statistical methods to find out the most valid procedure to achieve the desirable outcome.

Chapter 6

Differential Scanning Calorimetry (DSC) of Street Samples of Crack Cocaine

6.1. Introduction

Crack cocaine is a free base form of the illicit drug cocaine that is manufactured by various makeshift methods. Users take the drug in vapour form using home-made ‘crack pipe’ devices constructed from readily available items such as drinks cans, bottles and medical inhalers [84]. Some Drugs Services provide standardised pipes, mouth pieces, brass screens and chopsticks as a harm reduction measures [85]. The impact of distributing those measures on the rate of possible transmission of hepatitis C virus and to attract users into services has been evaluated [85].

The study of each pipe’s efficiency and the inhaled dose to the drug users required a study of the thermal behaviour of drug samples and the effect of cutting agents on their behaviour under smoking conditions. The thermal properties of materials are assessed by calorimetry procedures [86]. That shows relationships between the temperature and material’s specific physical properties [86]. Two main types of differential thermal instruments are commercially available, differential thermal analysis (DTA), and Differential Scanning Calorimetry (DSC). The principal difference between DTA and DSC is that DTA measures differences of temperature, whilst DSC measures differences of energy [87]. DSC is the prevalent technique that is widely applied due to its ability to provide information about the physical properties, and the energetic properties of the sample. DSC is a very widely used technique to study the changes in thermo-chemical properties and for the identification of polymorphism through heating and cooling. DSC can be used to measure glass transition, crystallisation, and melting point temperatures of a sample [87]. DSC shows substance transitions as a function of temperature and time, measuring quantitatively any heat that is absorbed or diffused from the samples depending on a temperature difference between the sample and a reference substance [86, 88].

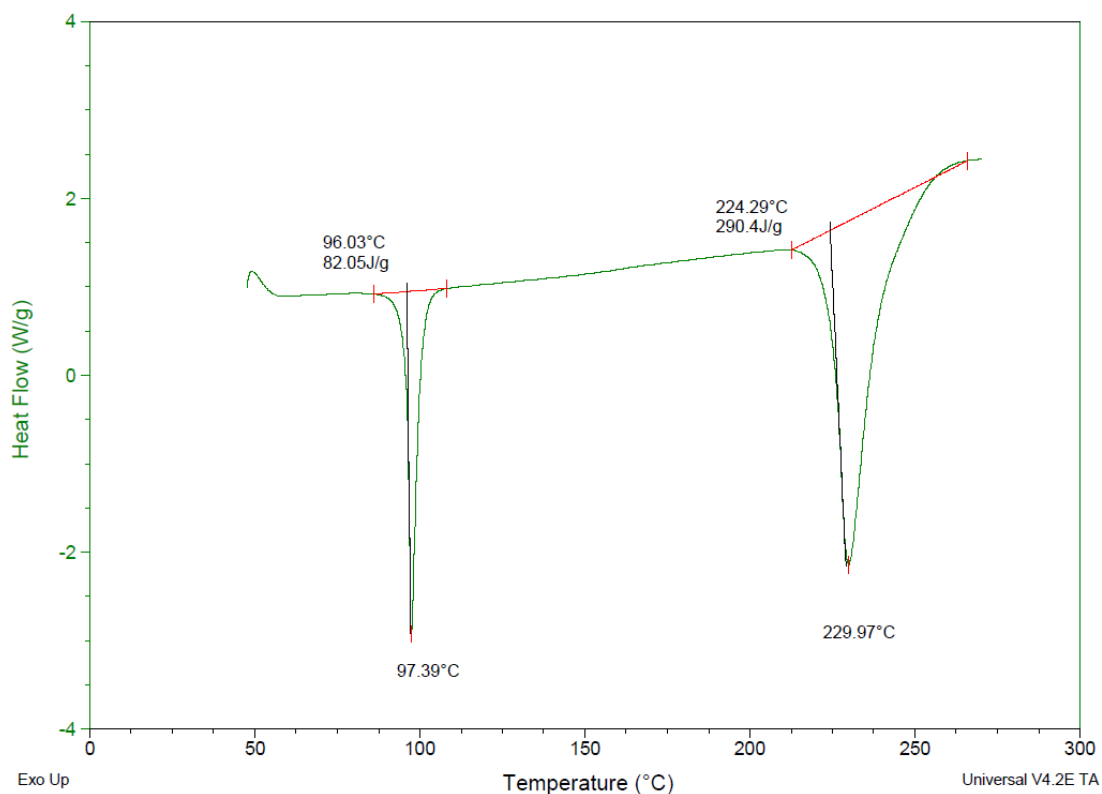
As preliminary to devising an experimental model of the crack smoking process, a DSC study of cocaine, street samples of crack cocaine and its common adulterants was undertaken. The only other previous DSC study [89] of cocaine HCl and

adulterants commonly used in the late 1980s, focused on the use of DSC as a method for the analysis of seized samples.

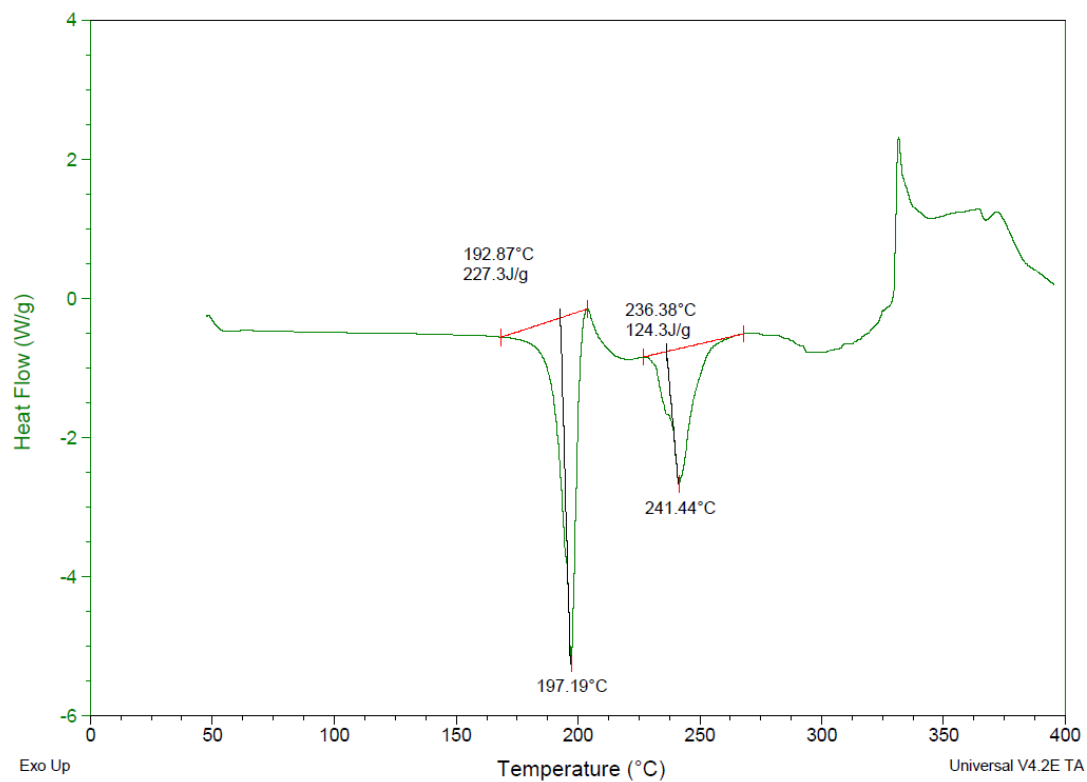
The purpose of the experiments reported here was to study the thermal properties of cocaine base and modern adulterants to examine the thermal behaviour of pure compounds, mixtures and street crack samples, and to choose the optimal temperature for studying the efficiency of different common devices for smoking cocaine.

6.2. Results and Discussion

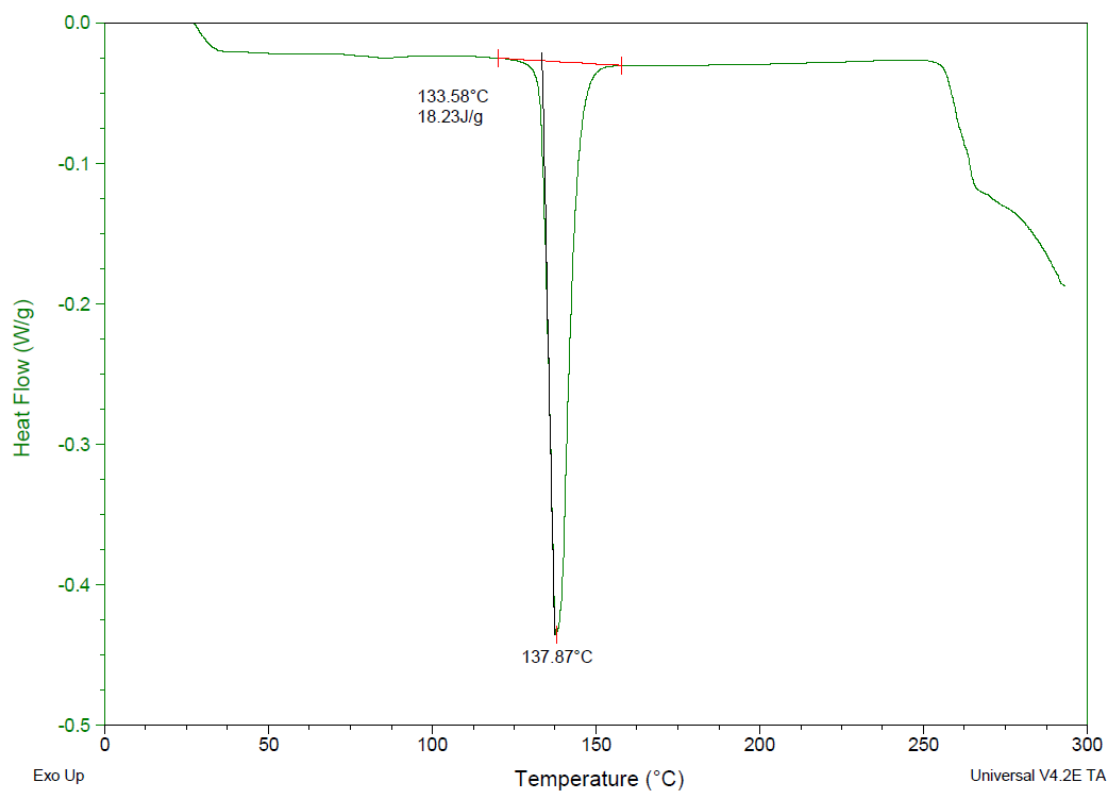
DSC scans of pure samples of cocaine HCl, cocaine base, phenacetin, benzocaine and levamisole HCl were obtained. All showed the expected endothermic peaks for melting, followed in some cases by evidence of thermal decomposition (Fig. 6.1). In Fig. 6.1, the thermogram obtained on heating cocaine base exhibited two endothermic peaks (peak 1 and peak 2) (Fig. 6.1.a). The first peak at 97.39 °C is the melting of the cocaine base, while the second endothermic peak at 229.97 °C may be a mixture of evaporation, and decomposition [56]. The second thermogram of cocaine HCl (Fig. 6.1.b) shows the difference in melting point and other thermal properties between the base and salt forms of cocaine. The third and fourth thermograms are for phenacetin and benzocaine (Fig. 6.1.c, 6.1.d) respectively. Phenacetin and benzocaine are two examples of common adulterants in crack cocaine samples. Phenacetin melts at a higher temperature than cocaine base whereas benzocaine melts at a lower temperature than cocaine base. The levamisole HCl thermogram (Fig. 6.1.e) shows the high melting point of levamisole HCl (231.80 °C) compared with cocaine base melting point (97.39 °C). The paracetamol thermogram (Fig. 6.1.f) shows the melting point at 172.32 °C.



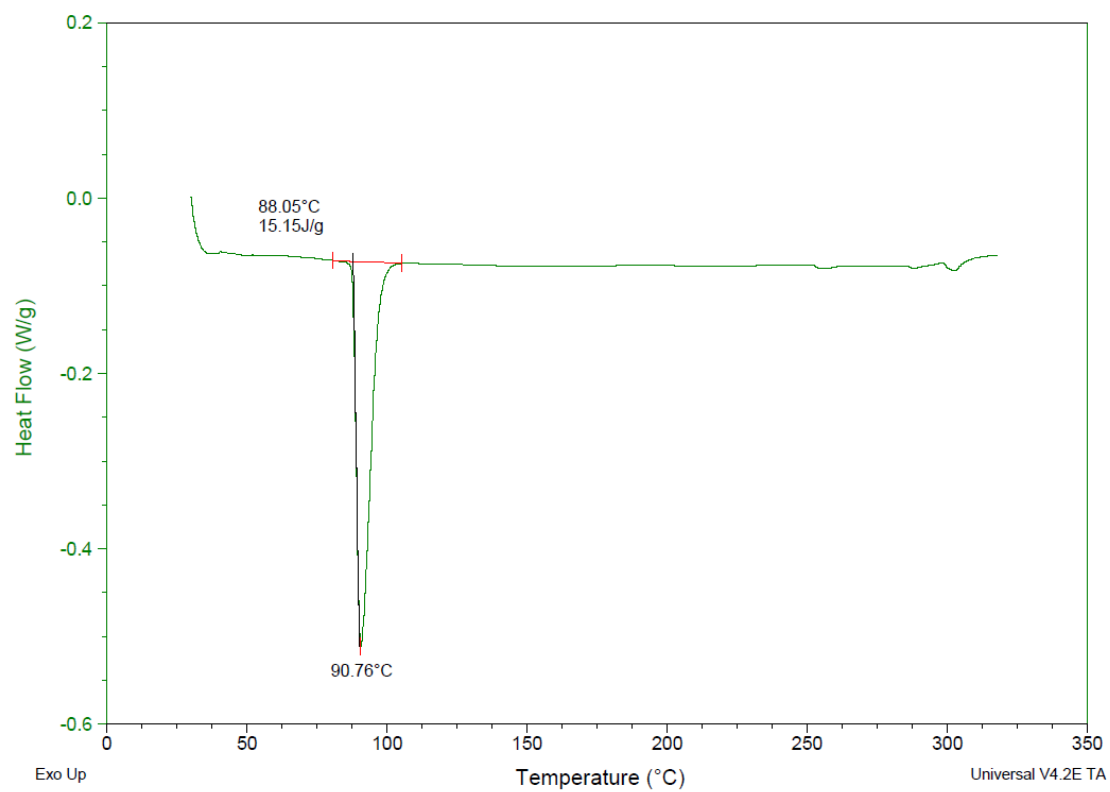
a. Thermogram of cocaine base.



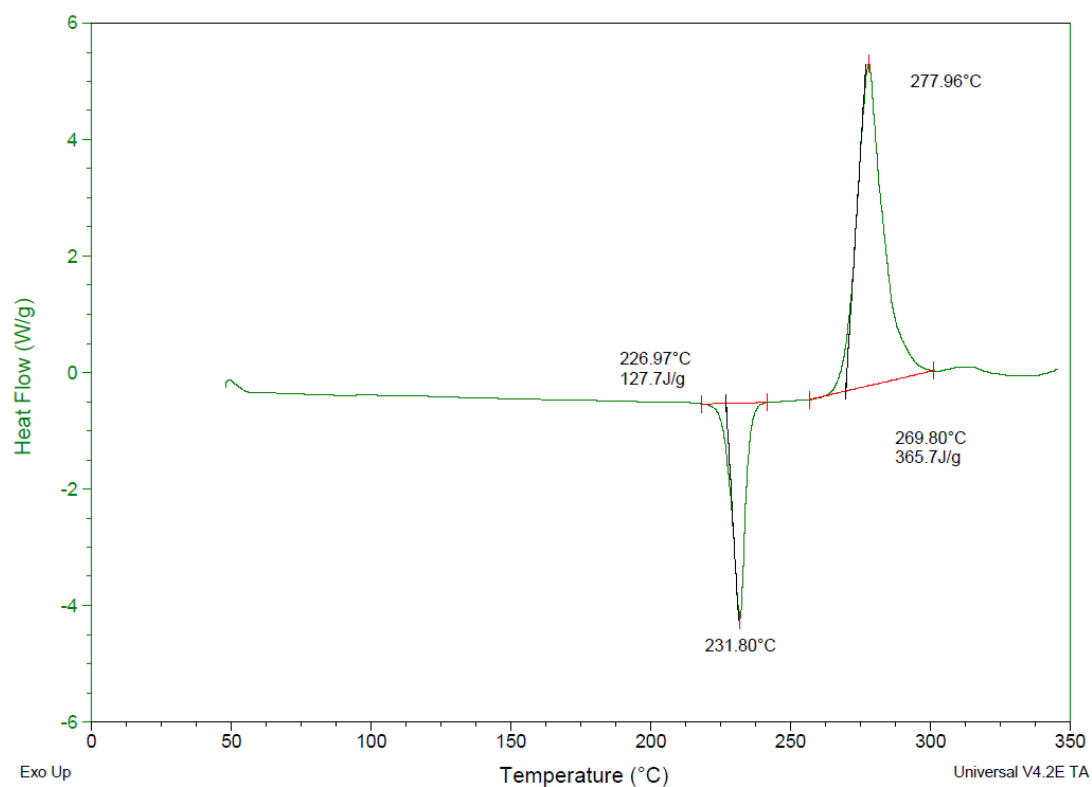
b. Thermogram of cocaine HCl.



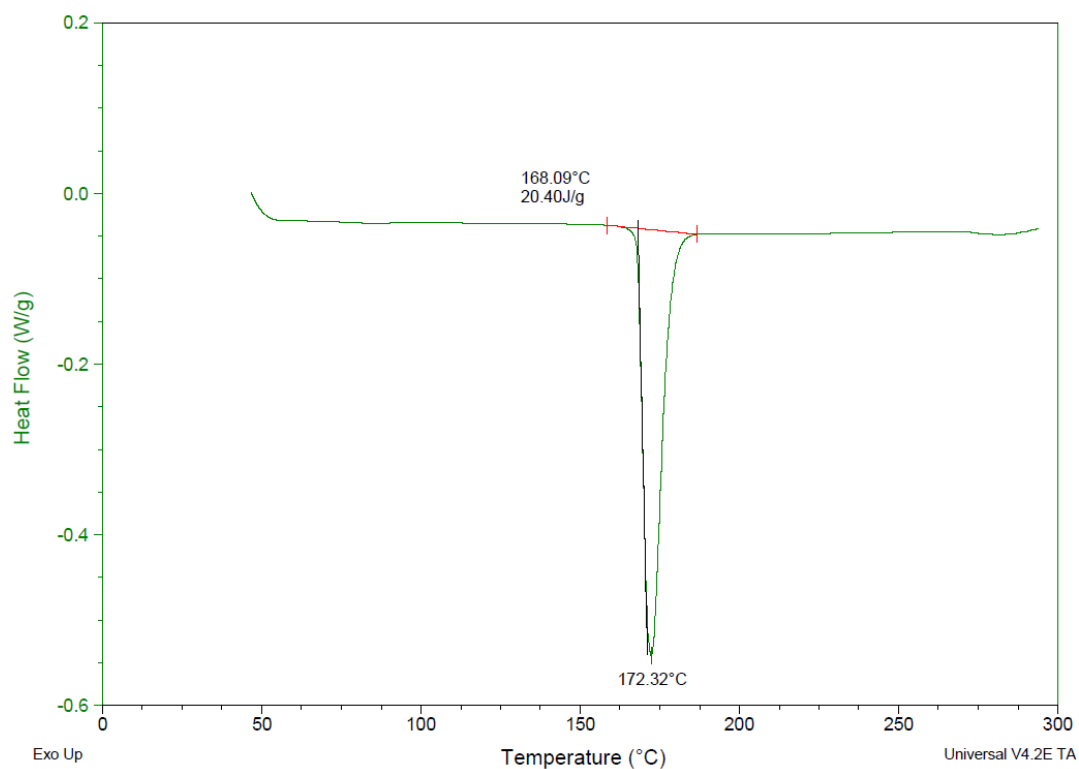
c. Thermogram of phenacetin.



d. Thermogram of benzocaine.



e. Thermogram of levamisole HCl.



f. Thermogram of paracetamol.

Fig. 6.1. Thermograms of cocaine base, cocaine HCl, phenacetin, benzocaine, levamisole HCl, and paracetamol.

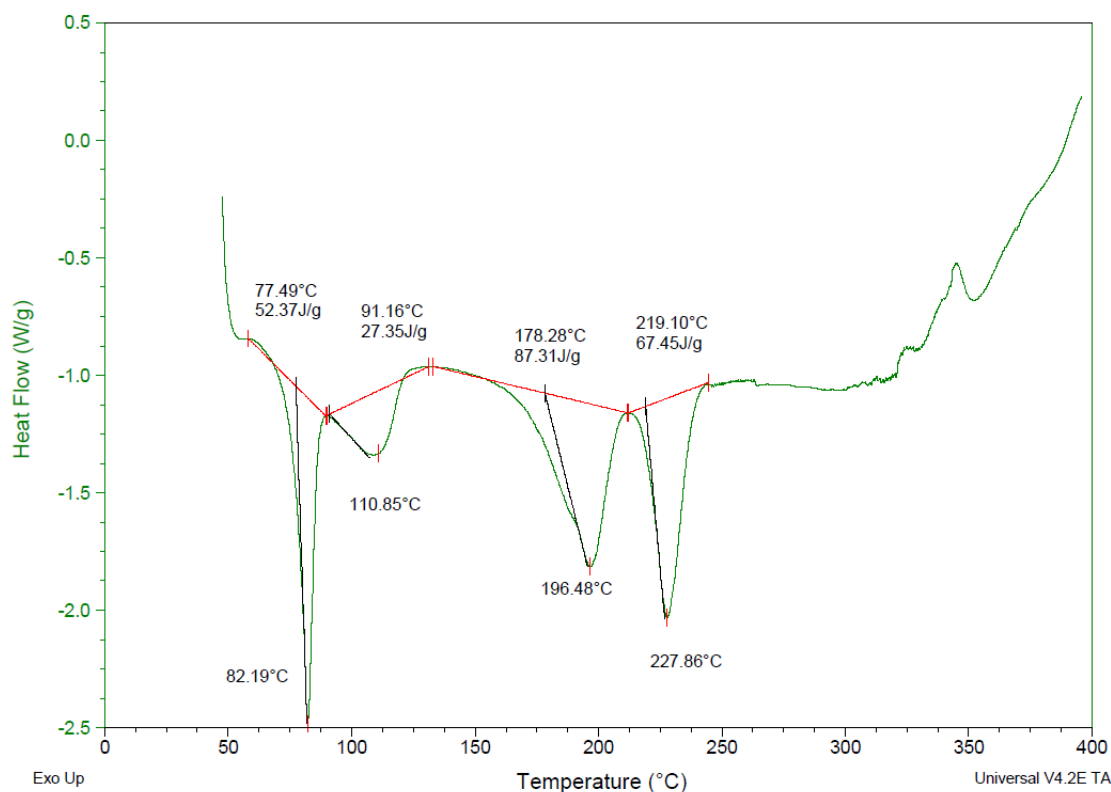
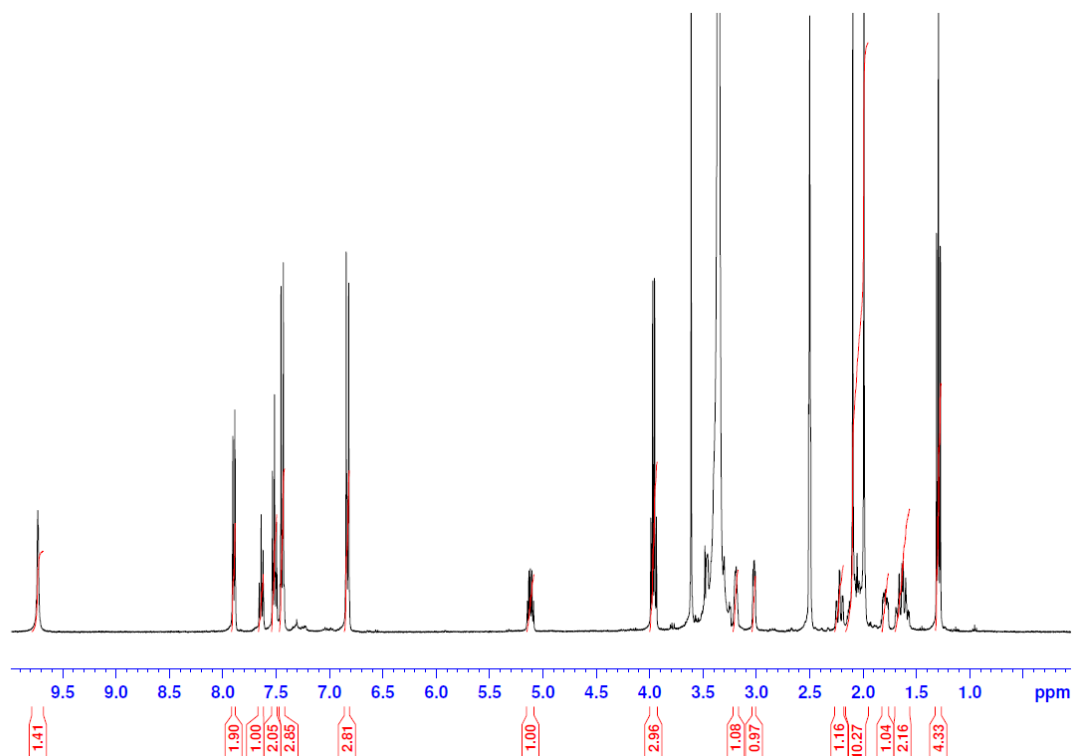


Fig. 6.2. DSC thermogram of Reference crack sample.

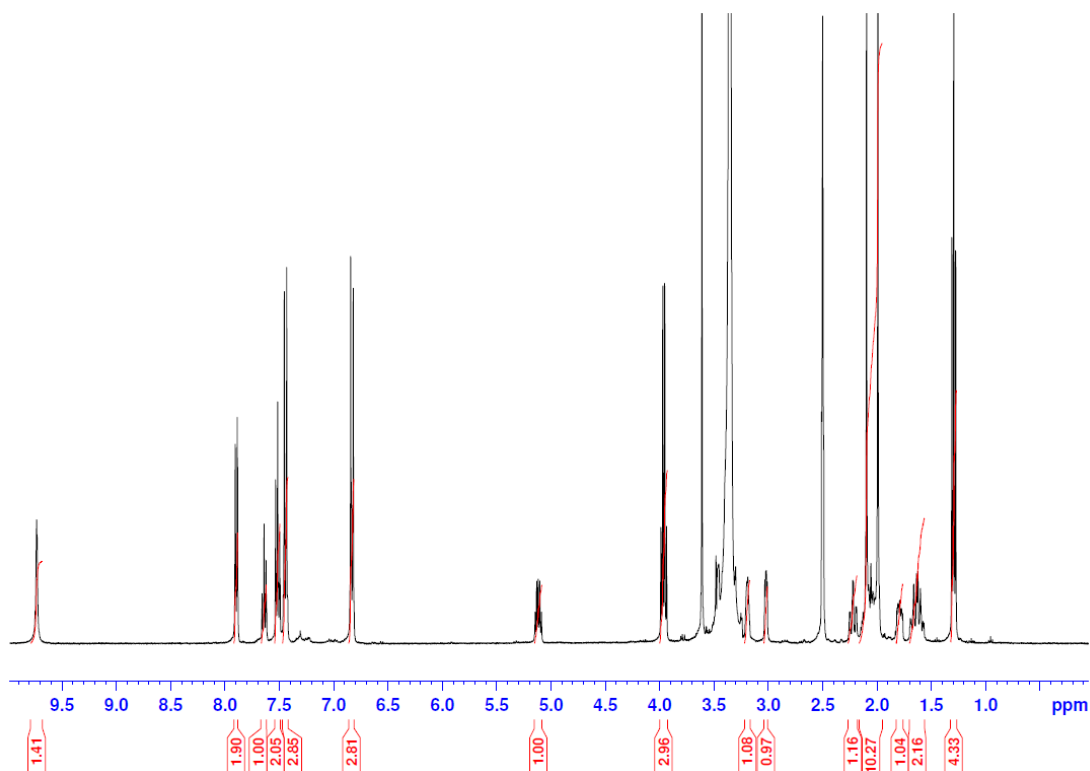
DSC scans of the street samples of crack cocaine generally showed a slight depression in the transition temperature of both cocaine base and the main adulterant (Fig. 6.2). Moreover, the scans also showed other complex features maybe related to other minor components in the mixtures or possible chemical reactions between components. The first thermal peak was an endothermic transition at 82.2 °C attributed to be melting of cocaine base. The next thermal peak was a broad endothermic peak at 110.85 °C attributed to be phenacetin melting. The DSC thermogram of the reference crack sample showed the interactions between cocaine and phenacetin. The melting point for cocaine base as pure substance is 97.39 °C, while in the crack sample the melting point is decreased from 97.39 °C as pure to 82.2 °C as adulterated by phenacetin. As well, the phenacetin melting point was shifted down from 137.87 °C with a sharp peak as pure substance (Fig. 6.1) to 110.85 °C with a broad peak as an adulterant with cocaine in the crack sample (Fig. 6.2).

The confirmation of chemical changes in the crack sample was obtained by NMR spectroscopy after stopping the DSC scan at certain temperatures. The first test was to compare the content of crack reference samples before and after DSC runs at 150 °C. The NMR thermograms show the identical peaks between the same sample

before and after the test (Fig. 6.3). This can be explained as the DSC peaks that appeared before 150 °C being due to melting.



a. Reference sample



b. Reference sample after DSC run

Fig. 6.3. NMR for Reference crack sample before and after DSC run at 150 °C.

Attribution of the peak at 196.48 °C in the DSC thermogram of crack cocaine, which could match the peak at 229.97 °C in pure cocaine base (Fig. 6.2), was carried out by heating the cocaine base samples to 275 °C, then examining the residue of the sample by NMR. The results obtained from the analysis of the NMR spectroscopy showed only a few peaks, while all of the cocaine assigned peaks disappeared in NMR spectrum. This could be explained by this peak being attributed to the total degradation of the cocaine content (Fig. 6.4).

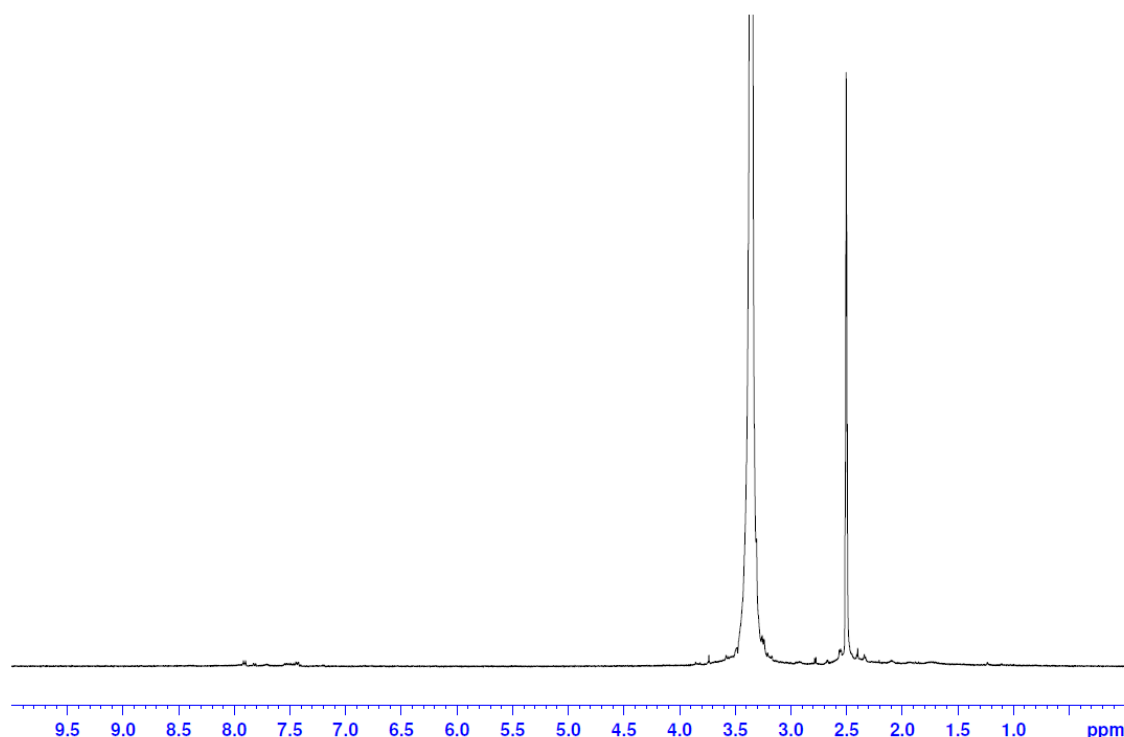


Fig. 6.4. NMR spectrum for cocaine base (residue after heating at 275 °C by DSC, DMSO).

6.2.1. Component concentration effects on thermal peak shifts in the mixtures

DSC thermograms for different samples that have the same components have various thermal behaviours depending on the concentration of each component. Studying the impact of concentration on the thermal behaviour may facilitate the interpretation of the behaviour of crack samples that have a variety of content and concentrations. A series of three mixtures that included cocaine and phenacetin were prepared and the DSC thermograms were run for each mixture three times under the

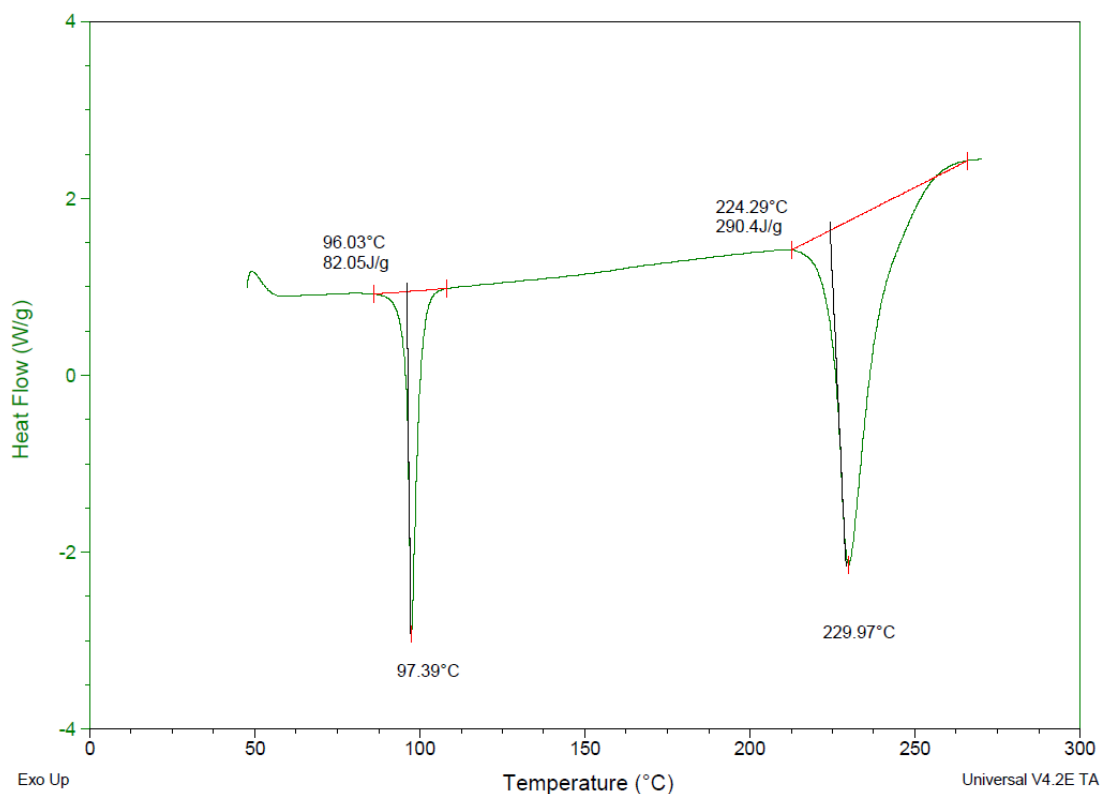
same conditions. The concentration of cocaine has decreased from 75 % in mixture 1 to 25 % in mixture 3, and vice versa for phenacetin. The mixture content is shown in Table 6.1. The melting points of pure substances are 97.39 °C and 137.87 °C for cocaine base and phenacetin respectively (Fig. 6.1.a, 6.1.c).

Table 6.1

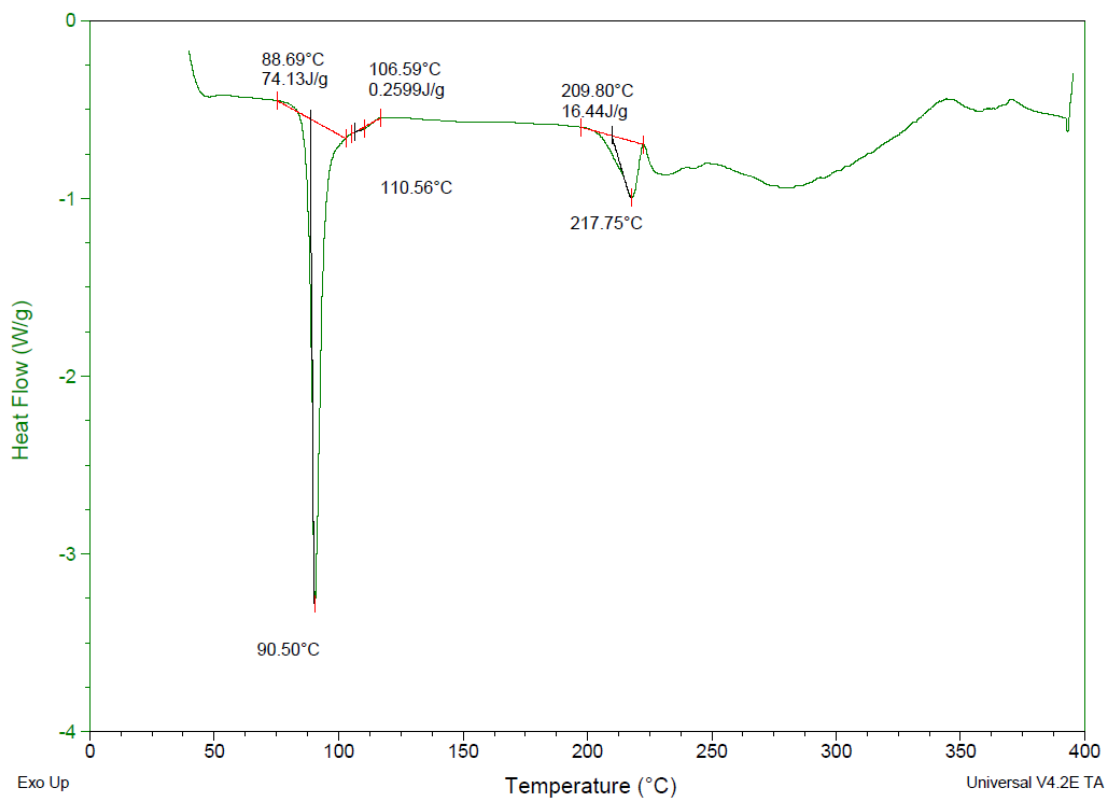
Content of cocaine and phenacetin mixtures.

| Mixture | Cocaine (%) | Phenacetin (%) |
|---------|-------------|----------------|
| | 100 | 0 |
| mix 1 | 75 | 25 |
| mix 2 | 50 | 50 |
| mix 3 | 25 | 75 |
| | 0 | 100 |

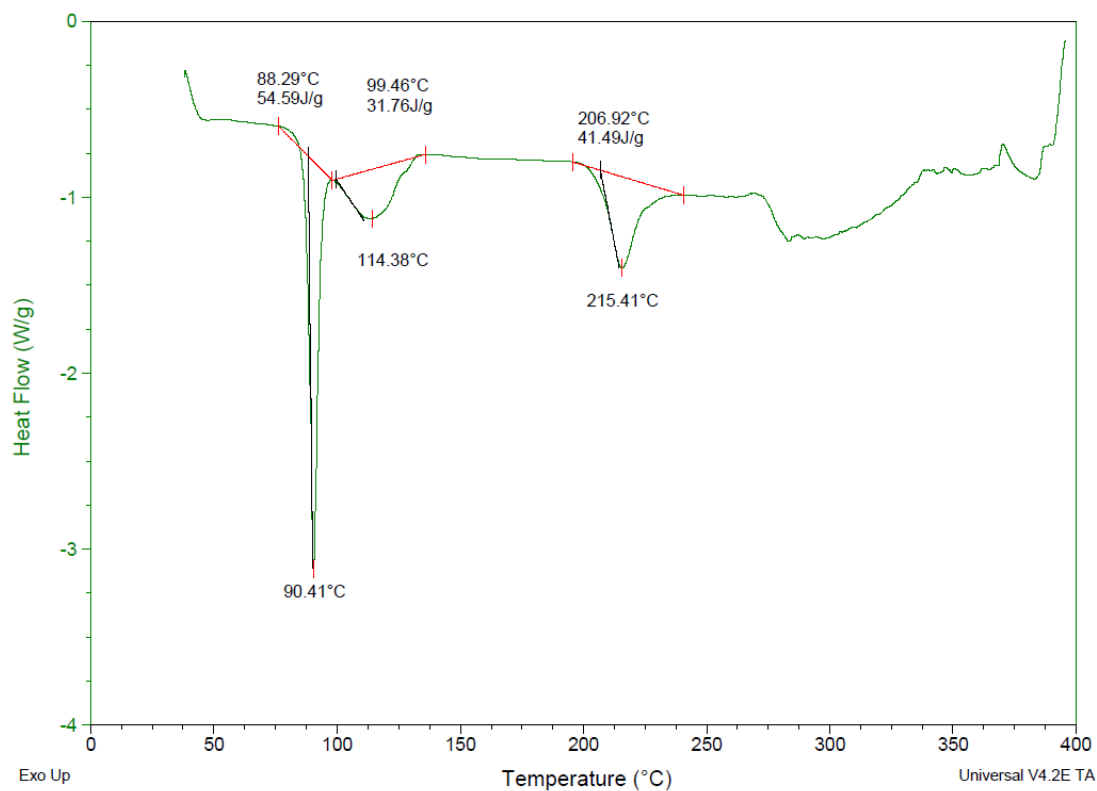
Mixture 1 was formed by adding 25 % of phenacetin to 75 % cocaine. Mixture 1 had a change in melting points peaks and shape for both substances. The thermogram obtained on heating mixture 1 exhibited two endothermic peaks (peak 1 and peak 2). The cocaine thermal peak became smaller and kept sharp, and it shifted down from 97.39 °C to 90.50 °C by adding 25% of phenacetin. Additionally, the peak for phenacetin has altered. The phenacetin melting peak appeared as a broad shoulder close to the cocaine sharp peak and it has changed from 136.39 °C as the pure substance to range 100-115 °C as 25 % in mixture 1 (Fig. 6.5). The thermograms of mixture 2 and 3 are presented in Fig. 6.5, and the details about mixture 2 and 3 are presented in Table 6.2.



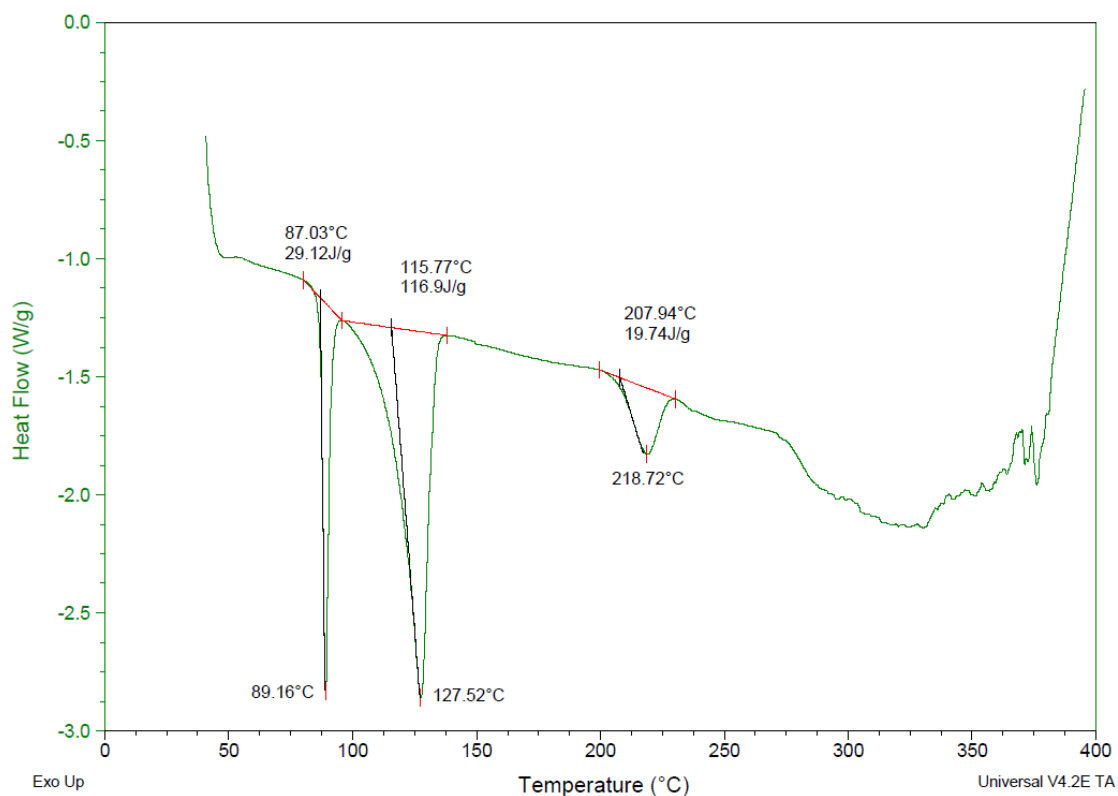
a. DSC thermogram of cocaine free base.



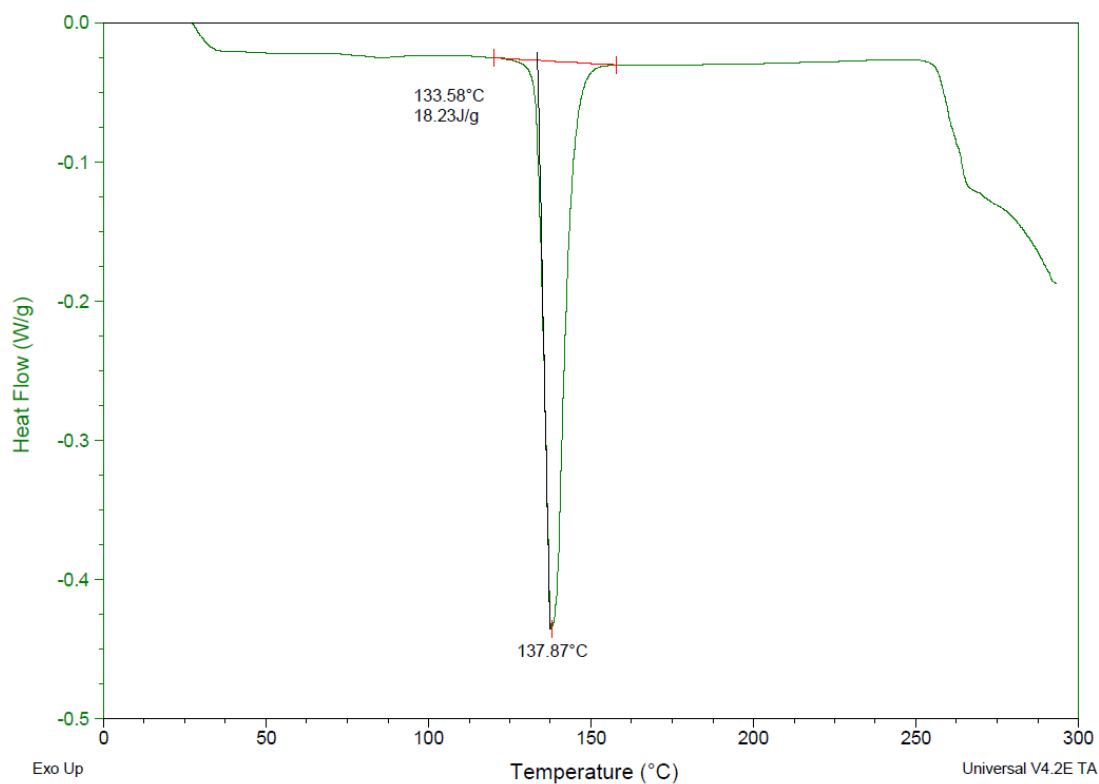
b. DSC thermogram of mixture of cocaine base and phenacetin (mixture 1).



c. DSC thermogram of mixture of cocaine base and phenacetin (mixture 2).



d. DSC thermogram of mixture of cocaine base and phenacetin (mixture 3).



e. DSC thermogram of phenacetin.

Fig. 6.5. DSC thermograms of mixtures of cocaine base and phenacetin.

Table 6.2

Results of DSC for mixtures of cocaine base and phenacetin.

| Mixture | cocaine | phenacetin |
|-----------------|---------|------------|
| | peak | peak |
| Pure cocaine | 97.64 | |
| mix 1 | 90.79 | 110.97 |
| mix 2 | 90.22 | 114.38 |
| mix 3 | 89.61 | 127.52 |
| Pure phenacetin | | 137.87 |
| Ref crack | 82.19 | 110.85 |

DSC was run three times for mixtures and then the average for the transition temperature and peak temperature were calculated. The results are presented in Table 6.2. They show how changes happened to phenacetin values, while changes are

smaller compared with cocaine ones. The changes in the peak temperature for cocaine and phenacetin are shown in Fig. 6.6.

Reference crack sample according to HPLC analysis contains 55% cocaine base and 45 % phenacetin. This concentration is close to the concentration of mixture 2 (50 % cocaine and 50 % phenacetin). The results in Table 6.2 show the differences in the thermal behaviour of cocaine and phenacetin between physical mixture and street crack samples. These differences may be caused by minor impurities depending on the origin of each components and the preparation method of street samples. This could show that even similar content crack samples could have different thermal behaviour depending on their content and preparation procedures.

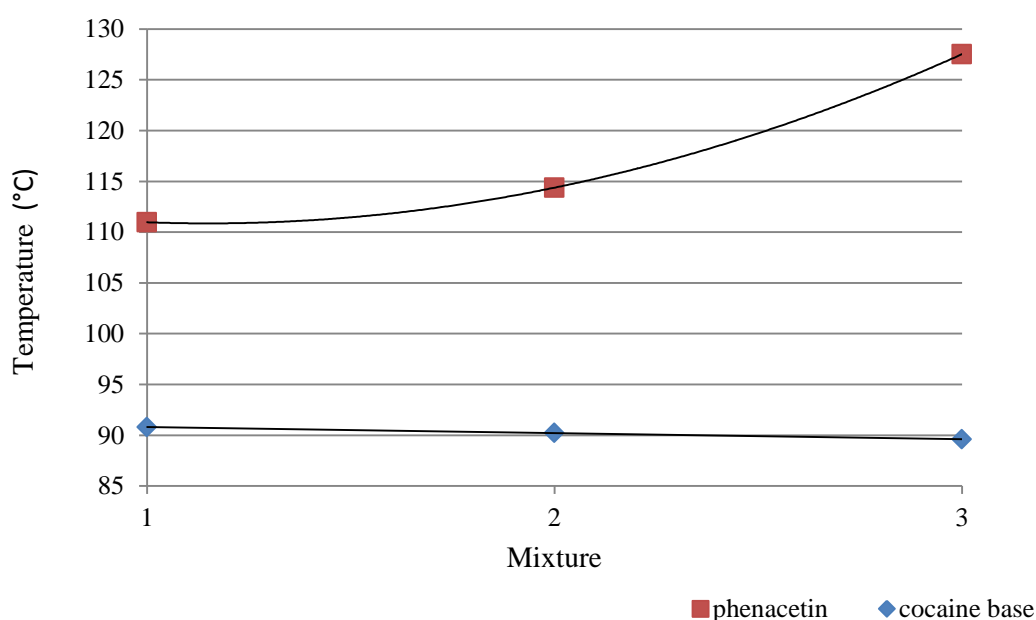


Fig. 6.6. Changes in cocaine and phenacetin melting peak temperatures.

6.3. Conclusions

Different street samples of crack cocaine gave markedly different DSC profiles, and it is likely that this significantly influences the thermal performance of the crack samples during smoking. From these findings it is concluded that, in general, there are many factors that can affect the thermal behaviour of the drug and the cutting agents. The concentration of each component can affect the thermal behaviour of the sample. The preparation method also has an effect. This was shown between crack

samples and physical mixtures of the samples prepared at the same concentrations. Therefore, different samples from different sources may have different thermal behaviour depending on the content, concentrations, and preparation methods.

The purpose of the current study was to determine the thermal behaviour of authentic and seized crack cocaine samples. It is clear that the use of too high a temperature during crack smoking will lead to loss of the drug by decomposition. These results were used in further experiments using the temperature to measure the efficiency of different common crack pipes used by smokers. Additionally, the degradation results could be delivered within harm reduction messages to drug users to avoid smoking more hazardous components which may cause more health problems. This is one of the suggested methods to minimize the problems associated with drug use habits. In the same way, the thermograms of crack samples have unique bar-codes that may refer to many parameters, e.g. major contents, minor contents, and preparation methods. These bar-code patterns could be used similarly to our concept for the possible use of chromatograms and spectra to link the changes between pure and impure cocaine with consequences harmful to health.

The limitations of this study are that most of the crack samples examined have the same cutting agent and that found at similar concentrations. Further experimental investigations are needed to estimate the effects of phenacetin at different concentrations, and to study the impact of other cutting agents on cocaine thermal behaviour. This can help to profile the samples and identify the components and the chemical forms of each one depending on the melting points and the shifts in impure samples. DSC is able to differentiate between similar samples. So this could be used in multivariate analysis as was applied to the NMR data. This can add more details to improve the power of clustering between samples.

Studying the thermal behaviour of crack cocaine samples will facilitate choosing the optimal temperature as one of the parameters from the smoking crack model in monitoring the efficiency of different common devices used by crack smokers and measuring the emitted dose of cocaine and cutting agents. The results of these experiments will now be delivered to crack smokers to inform them and to evaluate the impact of the results on users' knowledge.

Chapter 7

Crack smoking model

7.1. Introduction

Crack cocaine is inhaled in vapour form using home-made crack pipes constructed from readily available items such as drinks cans and bottles and medical inhalers. Some drugs services supply standardised pipes as a harm reduction measure [84]. There are few studies that discussed the analysis of crack cocaine samples or physical mixtures of cocaine and other cutting agents after volatilising. They tried to study the stability, thermal behaviour and decomposition and to measure the impact of experiments conditions and to quantify the recovered cocaine [56, 59, 61]. Gostic and co-authors focused on the thermal decomposition of adulterated cocaine samples which may have given more information about the thermal behaviour of samples [56]. There are two main parts in this study; firstly, they evaluated the recovery of the cocaine base and the impact of different adulterants on the recover through preparing physical mixture samples in the laboratory; secondly, they tried to detect any unique pyrolytic compounds. Procaine mixture recovery was higher than pure cocaine, while caffeine and phenacetin have negative effects on cocaine recovery, and benzocaine slightly improved the evaporation properties of cocaine [56].

Martin and co-authors studied the effect of temperature and flow rate on the pyrolysis of cocaine and the ratio of intact cocaine and other pyrolytic products recovered (methyl ecgonidine and benzoic acid) [61]. The vapour stream was passed through three traps containing ethanol, H_2SO_4 and NaOH , respectively. Cocaine and pyrolytic products were quantified in each trap at different conditions to measure the effect of these conditions and how the pyrolysis process ran. As the temperature was increased, the formation of pyrolysis products was increased, and when the flow rate was reduced, the formation of pyrolysis products was increased [61]. Many other pyrolysis products were identified at various heating conditions such as benzoic acid, methyl benzoate, *N*-methylbenzamide [90].

Due to the importance of pipes and their impact on the health of users, there have been several attempts to provide crack users with safer devices to reduce the harms that are associated with crack pipes. Hatsukami and co-workers studied the

ability to deliver exact doses of cocaine by special design. They prepared the cocaine in solution, dried the solution onto wires in the device for giving crack users. This enabled crack users using these devices to have accurate control of the amount of cocaine used [91]. One of the studies about supporting crack users with safer kits was done in Canada by Fischer and his research group [92], where cocaine is considered very prevalent in some Canadian cities. They studied the efficiency and barriers to distribute safer kits to reduce infectious and sexually transmitted diseases by sharing equipment. They categorized the benefits of distributing the kits into three groups: health, economic and social benefits. On the other hand, the main barriers for their project were: police enforcement, materials shortage and limited sources and distribution [92].

In this thesis, a study was designed to evaluate the efficiency of different crack pipes under conditions that mimic as closely as possible the actual practices of users and which take account the thermal behaviour of crack samples revealed by as described in the previous chapter.

7.2. Results and Discussion

7.2.1. Optimisation of crack smoking carried out

Three primary experiments were to control the parameters and to show the main differences at different temperatures (Table 7.1).

Table 7.1

Cocaine distribution in every stage as a percentage out of used cocaine sample.

| Expt. | 1 | 2 | 3 |
|-----------------|--------|---------|------|
| Temp range (°C) | 90-110 | 100-130 | +200 |
| stage 2 | 0.05 | 1.84 | 0.02 |
| stage 5 | 2.33 | 3.54 | 0.02 |
| shooter | 16.41 | 23.08 | 1.14 |
| trap 1 | 7.78 | 7.22 | 0 |
| trap 2 | 1.007 | 6.72 | 0 |

In Expt. 1 the applied temperature was in the range 90-110 °C. In Expt. 2 the applied temperature was between 100-130 °C. In Expt. 3, the applied temperature was higher, more than 200 °C, and the sample looked burnt inside the shooter.

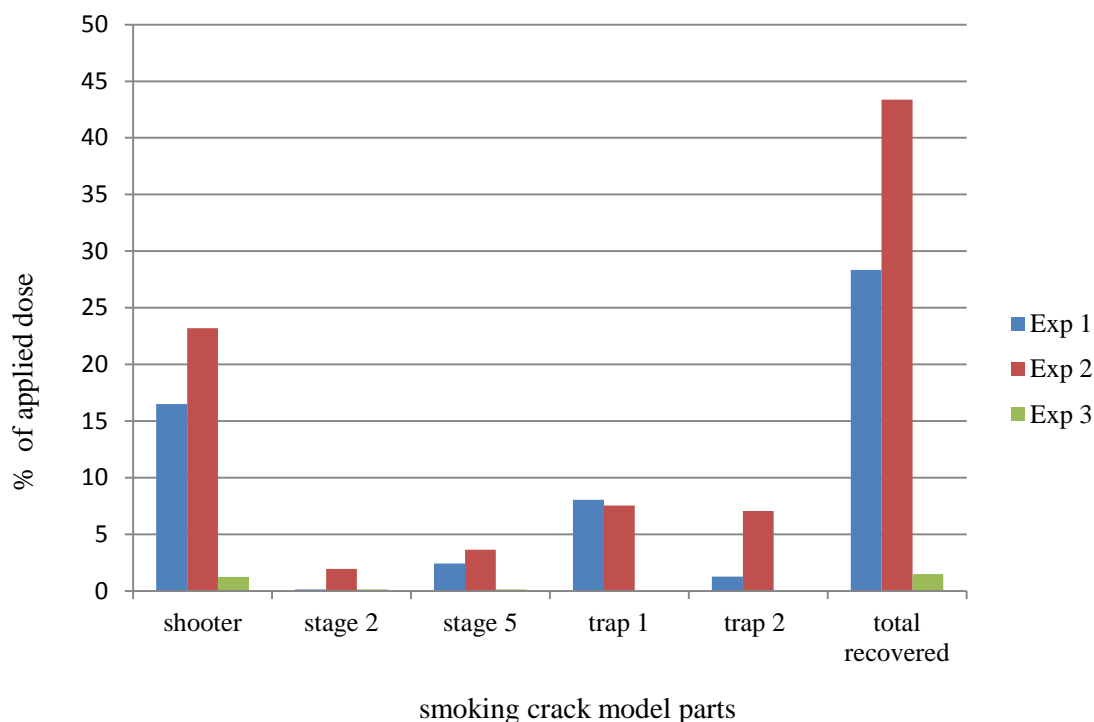


Fig. 7.1. The percentages of measured cocaine at each part.

Although, in Expt. 2, a high amount of cocaine is located in the shooter (Fig. 7.1), this experiment recovered the highest total amount of cocaine from other experiments (Fig. 7.1). These results validated the temperature that can be used to obtain the maximum amount to the optimized model, and so reduces the amount of crack cocaine that the users need every time they want to smoke by reducing the amount of waste. Overall recovery was less than 50 % and several possibilities were considered to explain these results:

decomposition of compounds. DSC results reported in the previous chapter showed a degradation peak for crack samples at ~190 °C. This would account for the recovery of cocaine in Expt. 3 being very low compared with those in Expts. 1 and 2 (Fig. 7.1);

volatilized cocaine may be not fully trapped;

some cocaine may be condensed in the tubes or on the inner surface of the ACI.

Accordingly the model was optimised by adding a third trap, all the tubing and the internal surfaces of the ACI were washed, and the compounds were measured in the modified operational procedure.

7.2.2. Behaviour of pure cocaine in crack smoking model

Using this modified model and procedure, four more experiments were run by applying a temperature of (100-130 °C) (Fig. 7.2) and Table 7.2.

The average amount of emitted dose was 51.8 % of the starting sample, while the averaged measured amount of cocaine base in the shooter was 15.5 % only (Table 7.2). The differences between results could be due to the manual heating of samples, uncontrolled factors such as the temperature of the laboratory where the experiments were done and personal factors because the heating is not a fixed or automatic process.

Table 7.2

The percentage of applied dose of cocaine measured at each part.

| Exp | shooter | stage 2 | stage 5 | ACI | trap 1 | trap 2 | trap 3 | tubing | Emitted into apparatus | total recovered |
|---------|---------|------------|------------|------|-----------|-----------|-----------|--------|---------------------------|--------------------|
| 9 | 21.0 | 0.1 | 2.2 | 6.3 | 13.6 | 17.4 | 1.3 | 2.6 | 43.4 | 64.5 |
| 10 | 29.9 | 0.3 | 0.2 | 2.6 | 10.6 | 19.8 | 1.6 | 5.2 | 40.3 | 70.2 |
| 11 | 7.3 | 0.7 | 0.2 | 12.1 | 28.3 | 8.9 | 1.3 | 3.1 | 54.6 | 61.9 |
| 13 | 3.8 | 1.0 | 1.9 | 10.0 | 37.9 | 11.3 | 2.3 | 4.6 | 69.1 | 72.9 |
| average | 15.5 | 0.5 | 1.1 | 7.7 | 22.6 | 14.4 | 1.6 | 3.9 | 51.8 | 67.3 |
| STDV | | | | | | | | | 13.0 | 5.1 |
| RSD | | | | | | | | | 25.1 | 7.5 |

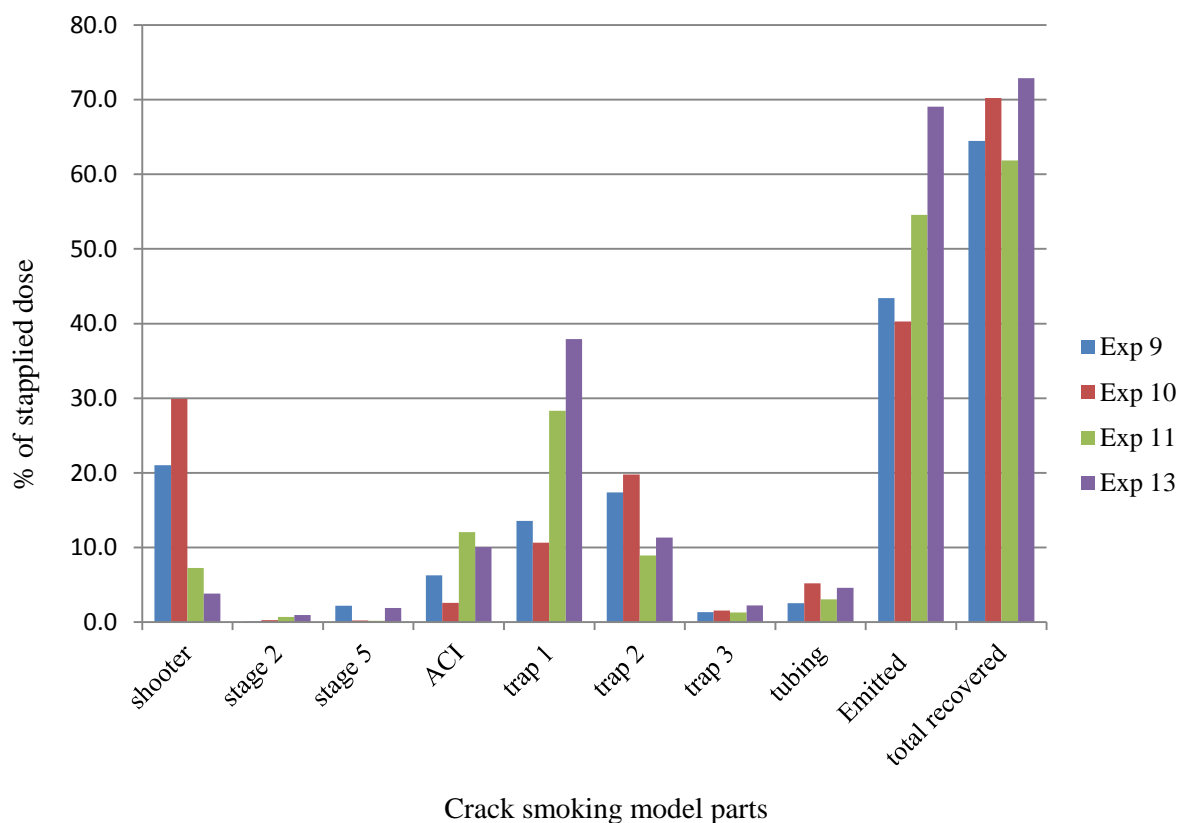


Fig. 7.2. The amount of cocaine base measured at each part.

7.2.3. Behaviour of street crack cocaine in the crack smoking model

Results from a series of experiments in which the reference crack sample was run are shown in Table 7.3.

Table 7.3

Distribution of cocaine and phenacetin at the parts of the optimised smoking model

| expt. | | pipe | stage 2 | stage 5 | ACI | trap 1 | trap 2 | trap 3 | tubing | emitted | total recovered |
|-------|------------|------|------------|------------|------|-----------|-----------|-----------|--------|---------|--------------------|
| 30 | cocaine | 19.3 | 0.3 | 0.1 | 0.0 | 11.4 | 13.3 | 8.9 | 2.3 | 36.2 | 55.5 |
| | phenacetin | 20.1 | 0.2 | 0.1 | 3.7 | 13.1 | 15.0 | 10.2 | 2.0 | 44.4 | 64.5 |
| 32 | cocaine | 6.7 | 0.3 | 0.2 | 6.3 | 15.8 | 10.7 | 5.2 | 1.7 | 40.3 | 47.0 |
| | phenacetin | 6.9 | 0.2 | 0.1 | 5.2 | 19.2 | 12.0 | 6.0 | 1.8 | 44.5 | 51.4 |
| 33 | cocaine | 14.7 | 1.0 | 0.2 | 7.8 | 12.0 | 10.6 | 5.7 | 3.4 | 40.7 | 55.4 |
| | phenacetin | 13.8 | 0.8 | 0.2 | 7.2 | 16.0 | 12.1 | 6.7 | 4.0 | 47.0 | 60.8 |
| 34 | cocaine | 29.1 | 0.8 | 0.2 | 10.5 | 8.6 | 6.6 | 3.0 | 5.6 | 35.3 | 64.4 |

| | | | | | | | | | | | |
|---------|------------|------|-----|-----|-----|------|------|-----|-----|------|------|
| | phenacetin | 33.7 | 0.6 | 0.2 | 8.8 | 10.3 | 7.8 | 3.7 | 8.2 | 39.7 | 73.5 |
| 35 | cocaine | 7.0 | 0.4 | 0.2 | 7.9 | 13.3 | 9.6 | 5.6 | 5.1 | 42.1 | 49.1 |
| | phenacetin | 7.4 | 0.4 | 0.2 | 7.6 | 15.8 | 11.0 | 6.7 | 8.2 | 49.9 | 57.2 |
| average | cocaine | 15.4 | 0.5 | 0.2 | 6.5 | 12.2 | 10.2 | 5.7 | 3.6 | 38.9 | 54.3 |
| | phenacetin | 16.4 | 0.5 | 0.2 | 6.5 | 14.9 | 11.6 | 6.7 | 4.9 | 45.1 | 61.5 |

The experiments (Expts. 30, 31-35) were run at temperatures (100-120 °C) with advice from a harm reduction worker that users seek to minimise the temperature consistent at which they smoke crack. The range of emitted cocaine was 35.3 % to 42.1 %, while the emitted phenacetin under the same conditions was 39.7 % to 49.9 %. On the other hand, the amount of cocaine which was measured in the shooter after the run was in a range between 6.7 % and 29.1 %; and for phenacetin the amount of measure in the shooter was 6.6 % and 33.7 %. This does not agree with Gostic's results about the thermal decomposition of adulterated cocaine samples. Gostic estimated that the recovery of the phenacetin as an adulterant in his samples was $95.4 \% \pm 1.6$. This difference could be interpreted as being due to the difference in the samples, Gostic used a mixture of cocaine and phenacetin rather than a street sample as used in this study. As reported in the previous chapter, DSC scans provide evidence of a difference in the thermal behaviour of artificial mixtures compared with crack samples [56].

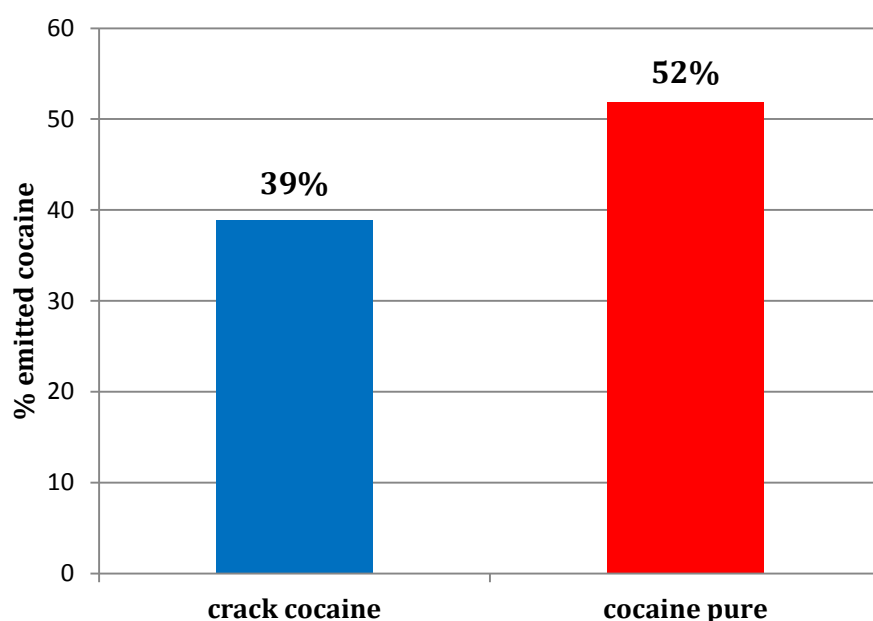


Fig. 7.3. Negative effect of phenacetin on the estimated emitted dose of cocaine.

The results of these experiments (Table 7.2) agree that phenacetin has a negative impact on the recovered amount of cocaine [56]. Under the condition of smoking crack, the estimated amount of emitted cocaine in cocaine pure samples is 51.8 %, while this percentage decreased by third to 38.9 % in the case of crack samples (Fig. 7.3). This information that the cutting agent of crack with phenacetin reduces the efficiency of crack smoking compared with pure cocaine may be of value in devising an intervention to inform drug users.

7.2.4. Comparison between different tools used to smoke crack cocaine by drug users

Various home-made tools are used by crack users to smoke crack cocaine which may differ in efficiency due to differences in design and application. Experiments were carried out in this study to measure the efficiency of three typical devices converted into crack pipes: drink cans, asthma inhaler, and standardized pipe.

These experiments aimed to measure the emitted dose for cocaine as drug and phenacetin as adulterant to smokers' respiratory systems and to measure the wasted amount in each device. Each was run in triplicate using the same sample (reference sample). In the case of the inhaler and drink cans, cigarette ash was used to load the crack sample. This process was more difficult to control compared with standardised pipe in which the sample was loaded on the metal "brillo" piece. Using cigarette ash increases the associated harm to crack smokers; this ash adds more toxins and harms beside the harms associated with crack cocaine smoking [93]. The results clarify that there was a lower emitted dose collected from using drink cans compared with the emitted dose from both the standardised shooter and inhaler (Table 7.4). The reason behind the lowest values in the case of using drink cans may be due to the difficulty of controlling the experiment and applying the thermometer and heating resource to the sample.

The emitted cocaine dose from all devices tested proved that the phenacetin has a negative impact on the emitted amount of cocaine under smoking conditions. This agrees with another study that used a mixture of cocaine and phenacetin under stability test conditions [56].

The graphs show the distribution of collected material from different parts of the smoking model. This can give an idea about the depth that cocaine and phenacetin can penetrate into a smoker's respiratory system. The largest amount of cocaine and phenacetin were collected as vapour from trap 1, which means that this amount will

be in touch with the huge internal surface of the lung and may be absorbed into a smoker's circulation. This may explain the fast response and stimulation of smoking crack compared with snorting [94] and injecting [95].

Table 7.4

Comparison between efficacies of drink cans, asthma inhaler, and standardized pipe.

| Expt | drink cans | | shooter | | inhaler | |
|---------|------------|------------|---------|------------|---------|------------|
| | average | | average | | average | |
| | cocaine | phenacetin | cocaine | phenacetin | cocaine | phenacetin |
| device | 7.3 | 9.6 | 15.4 | 16.4 | 8.8 | 10.3 |
| stage 2 | 0.8 | 0.6 | 0.5 | 0.5 | 0.7 | 0.6 |
| stage 5 | 2.0 | 1.9 | 0.2 | 0.2 | 0.3 | 0.3 |
| ACI | 7.7 | 6.1 | 6.5 | 6.5 | 9.0 | 9.1 |
| trap 1 | 6.2 | 8.3 | 12.2 | 14.9 | 16.8 | 19.7 |
| trap 2 | 6.1 | 6.9 | 10.2 | 11.6 | 14.8 | 18.3 |
| trap 3 | 2.4 | 2.8 | 5.7 | 6.7 | 5.2 | 6.2 |
| tubing | 6.2 | 7.2 | 3.6 | 4.9 | 0.1 | 0.2 |
| emitted | 31.2 | 33.7 | 38.9 | 45.1 | 46.8 | 54.3 |

Less than 1 percent of the starting sample was collected from stage 2 in the ACI. This stage filters particles that have diameter larger than 4.7 μm , which may be found or trapped in the upper parts of the respiratory system. The standardised pipe and inhaler provide the users with less than half of the cocaine in the sample while the drink cans provide them with only third of the cocaine. The rest of the cocaine was detected in the device (Fig. 7.4), wasted in the side-stream or degraded by heating [90]. The differences between cocaine collected from the different parts of the crack smoking model for drink can and shooter ($p = 0.37$) ($p > 0.05$), also for drink can and inhaler ($p = 0.4$), and for shooter and inhaler are not significant ($p = 0.95$).

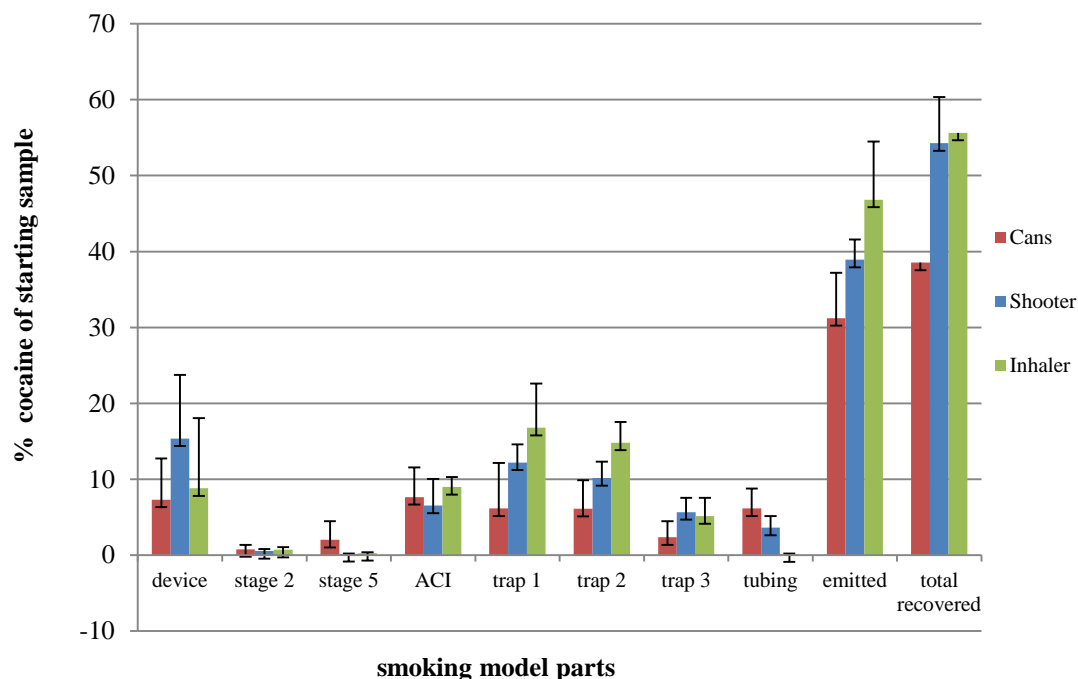


Fig. 7.4. Comparing cocaine distribution in the smoking model between three devices.

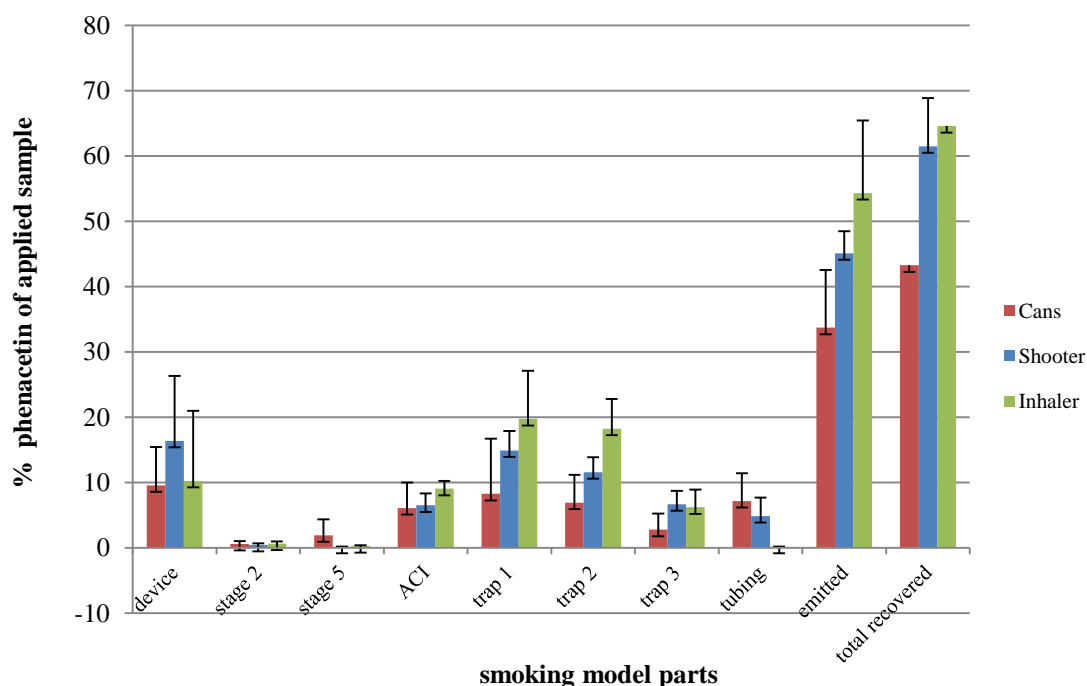


Fig. 7.5. Comparing phenacetin distribution in smoking model between three devices.

In total, the inhaler can provide more than half of the phenacetin into users, while both standardised pipe and drink cans provide less than 50 % of the phenacetin into users. Less phenacetin emitted to crack users can reduce the harms associated with phenacetin smoke. The collected amount of phenacetin in the device was 9.5 %

and 10.2 % in drink cans and inhaler respectively; on the other hand, the amount of phenacetin recovered from the standardised pipe was 15.3 % (Fig. 7.5). Many studies refer to phenacetin as one of the most common adulterants for crack cocaine [19, 22], but little is known about its potential toxicity via the inhalation route of administration. The present study shows that phenacetin used as a cutting agent in crack cocaine is delivered to the user as efficiently as the cocaine itself.

Previous studies reported degradation products of heating cocaine which are highly toxic, e.g. methyl ecgonidine (anhydroecgonine methyl ester, AEME), and ecgonine [90,96]. In order to detect potential degradation products, samples from the ACI were collected in methanol and analysed by mass spectrometry electrospray (Fig. 7.6.a, 7.6.b). Figure 7.6.a contains the peaks for cocaine and phenacetin of starting sample, while figure 7.6.b contains the peaks of phenacetin and pyrolytic cocaine products e.g. methylecgonidine and ecgonine. The studies usually tested the stability and the thermal behaviour of cocaine at high temperature. In the case of the optimised smoking model, the conditions of the experiments mimic the conditions of real crack smoking. Their results show that crack users are also exposed to these toxic products, and that smoking crack cocaine is therefore more risky [96]. The differences in the intensities between the two figures (Fig 7.6.a, 7.6.b) emphasize that the major emitted compounds are still cocaine and phenacetin, while the pyrolytic compounds are too minor compared with cocaine and phenacetin.

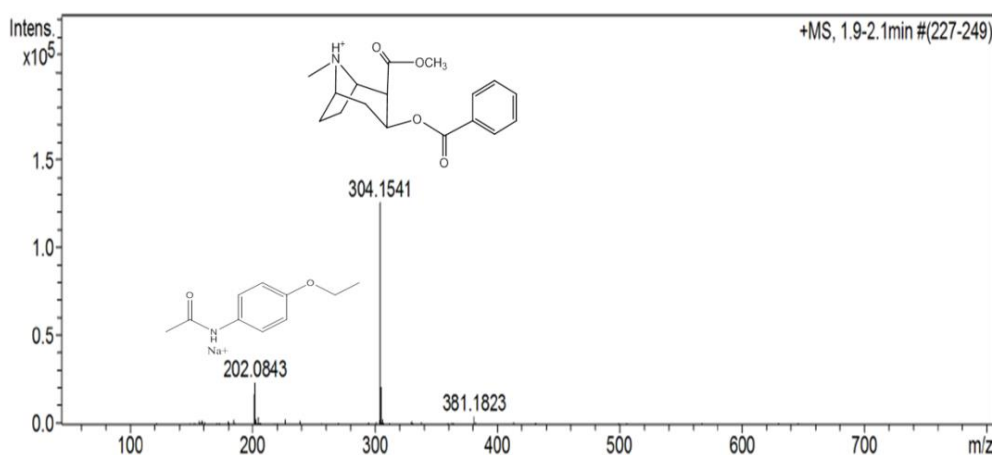


Fig. 7.6.a. The MS of a methanolic solution obtained from the smoking model (ACI)

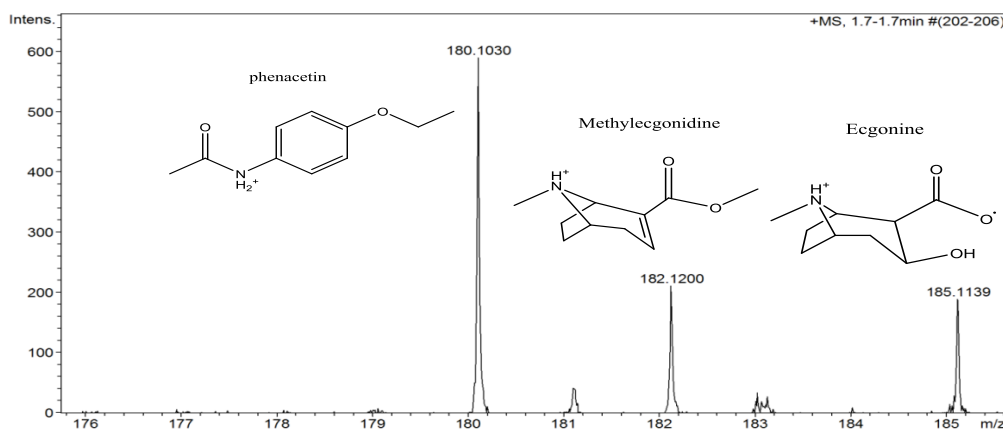


Fig. 7.6.b. The expansion of MS of minor peaks in the range between 176-185 m/z of the MS of a methanolic solution obtained from the smoking model (ACI).

7.3. Conclusions

Illicit crack cocaine is taken by various routes. One of the main routes is by inhaling the vapour through a makeshift crack pipe. The efficiency of this means of administration, and the effects of heating on the cocaine base and adulterants in the crack under smoking conditions, are not reported in the literature. Thus, an experimental model of crack cocaine smoking has been devised and used to investigate the vapour likely to be inhaled from a street sample of crack. On average 38.9 % of the cocaine base and 45.1 % of the phenacetin adulterant in provided samples were recovered from the vapour by using a standardised pipe. Also, 15.3 % of the cocaine base and 16.3 % of the phenacetin were recovered from the pipe (Canadian shooter) in the same experiments. Highly toxic pyrolytic products of smoking cocaine base were identified under smoking conditions. The results of these experiments into the variations between different tools and the emitted dose of cocaine and adulterants were used to design a harm reduction intervention. More than half of the samples were wasted in different ways which may encourage the users to use other route of administration to use crack. However, the smoking route is considered to be safer than other routes such as injection, so more experiments are required to optimise the conditions of smoking to reduce the waste. The smoking model reported here could be extended to samples with different cutting agents to validate the results in the case of other adulterants in seized samples.

Chapter 8

Literature Review - Pharmacy Practice aspect

8.1 Harm reduction (HR)

8.1.1 HR theory

The main aim of this review is to provide a basis from the literature to advocate the application of strategies of harm reduction (HR) for interventions aimed at drug users, especially at crack users. HR has become a central strategy to handle some problems that are associated with drug use. The principles of HR direct its practice as well as those principles that are accepted in prevention, public health, and behavioural change. The diversity of practice of HR may result from the definition of the problem and the expected successful intervention to solve it.

A main frame of the literature review will be related to HR focusing almost exclusively on drug use, its associated problems, and educational, information interventions of behaviour change. Also, some selected papers that discuss the history of HR and dependent policy applications will be briefly reviewed [30].

8.1.2 Practice and history of HR

HR is a group of principles and approaches related to human behaviour. HR aims to minimize the harmful effects of high-risk behaviours, e.g. drug use, alcohol abuse, and unprotected sex when HR is involved in a prevention or treatment program at individual or community levels [30]. The HR approach has been called different terms such as damage limitation, casualty reduction, harm minimization [26, 97], or risk reduction [98]. In any community, where people have possible contact with drugs, the non-medical consumption of psychoactive drugs cannot avoided [97] and it is a complicated phenomenon that ranges from abstinence to severe addiction. HR is focused on decreasing abuse, lessening intense use, and the negative effects correlated with use without necessitating immediate cessation of drug use [99]. HR is an evolving strategy to substance abuse and HIV prevention and treatment interventions that is increasing from the want for a conscientious response to substance abuse other than fulfilling the criminal law and imprisonment [100]. HR uses a series of

principles and hypotheses about how changes can be made by people in their lives and communities [100].

HR confirms people as the fundamental factor in bringing about decline in the negative effect from their high risk behaviour and establishing the fitness of individual and community life and prosperity. It is not simply stopping all high-risk behaviours, as the principle of evaluating successful interventions [98].

The reliable use strategy for alcohol education was grown in the early 1970s. It was one of the earliest implementations of a HR approach [26]. Moreover, methadone maintenance programs were launched in the United States in the 1960s. These programs are early examples of HR. Principal HR applications started in Amsterdam in the beginning of the 1980s as a reaction to widespread health problems linked to drug injection misuse [101]. However, in Amsterdam, the first needle exchange program started in 1984. It was established by “Junky Union,” a known organization of injecting drug users [100]. Later on, needle exchange programs (NEPs) started in the United Kingdom and in Sweden in 1986 [102]. Then, HR strategies started to spread into other countries, e.g. Canada, New Zealand, Australia, Thailand, Nepal, and to other European countries [103]. The first American NEP started in Tacoma, WA, in 1988. The distribution was carried out either legally by health departments or clinics, or illegally by AIDS activists [98].

8.1.3 An HR Framework and Approach

There is no literature consensus about the definition of HR, but there are some themes that merge together to form the known principles for understanding the HR approach. The fundamental elements of this framework include: overall approach, social context, understanding drug use, nature of interventions, definition of the problem, and definition of success. HR represents both a policy strategy and a group of interventions, making it difficult to reach a consensus HR definition [104].

One of the first elements is the approach itself. Researchers have discussed the HR approach and they described it as pragmatic [97, 105]. There is strong evidence from the literature of searching for applicable solutions for the negative impacts of problems associated with drug use. This approach gives an impression that what is required is not to ignore drugs and drug users, but the desired approach is to help users to learn how to live safely and healthily when they use drugs, thus HR.

The second commonly discussed term in defining the HR approach is a low-threshold aspect. The meaning of this term is that the HR supporter, according to HR approaches, provides help to users as they are, rather than where they should be [105]. The third term is non-judgmental. It discusses the idea of the aim of HR being to understand harms related to the risky behaviour itself and how to minimise it, not to enforce judgement on people or their behaviour [100, 104].

One of the main principles of HR strategies is working within a framework to achieve planned goals within an order that has hierarchy. HR aims to focus on targeted individuals and groups, and to implement direct and realistic goals to address the most risky problems. In the case of behaviours such as drug abuse, alcohol abuse, and high risk sexual behaviours, the HR approach presents those behaviours on a continuous scale ranging from severe abuse to total abstinence. The target of HR approaches is to shift the users toward abstinence, so this will be associated with decreasing the harms resulting from the behaviours. Abstinence will be the ideal result of a risk reduction approach. For that, any shift on this scale toward abstinence or less harm is considered as an improvement even if abstinence is not achieved [98].

One of the key features of HR is to have a comprehensive understanding to public health problems. This can improve the ability to design a more effective framework suitable to reduce the problems linked with specific behaviours [104]. For example, in the case of HR interventions for alcohol abuse, the harms that are associated with it are three types: violence and injury, road accidents due to drink driving, and social harms [104]. Furthermore, in the case of tobacco, the aim of HR is to make tobacco products that are safer, producing fewer harms to smokers and non-smokers [104, 106]. In this area, various kinds of HR interventions were identified: cigarettes with less emitted toxicants, cigarette-like products, smokeless tobacco, and prevention from environmental tobacco smoke [104].

The interventions of HR concerning illicit drug use are focused mainly on harms associated with injecting drugs, e.g. highly infectious blood-borne viruses (BBV) (HIV and HCV), overdose, and other injecting related harms [104]. A commonly used HR intervention is a needle-syringe program (NSP). The main aim for NSPs is to decrease the prevalence of BBV, while a secondary aim for NSP is to grow the access of drug users to services of HR support and treatments [104]. However, there were some negative suspected effects of operating NSP such as increasing the total number of drug injectors due to the ready availability of needles,

forming a community approach that lowering acquired risks may increase the number of drug users. However, the evidence concluded by researchers did not support those fears [104, 107, 108], and there was no evidence that crime increased where the NSPs were implemented [104, 108, 109].

The development of HR was categorised by Erickson [110] into three stages. He summarized the first stage as increasing the awareness of the negative effects of consumption of tobacco and alcohol at the users' level. The second stage according to Erickson started in 1990, when the first international conference on HR was held in Liverpool, UK. At that time, the increasing consciousness about the HIV epidemic and the increased thinking of transmission of HIV via contaminated syringes and needles had begun in 1983-1984. This fatal situation had shifted the movement into clean injection equipment from the criminalised, banned situation. One of the main HR factors to widen the application of HR interventions was the diversity of approaches of participants in HR including: drug users, front-line workers, and policymakers. Finally, the third stage was to develop an integrated approach of public health for both illicit and licit drugs. The impacts of health and criminal consequences are significant and this makes it hard to achieve any preventing policies if there is access to some drugs while others are banned. The objective of HR was to focus on the serious harms related to specific drugs and to get them reduced [110].

On the other hand, the arguments of HR advocates are summarised, according to Mangham [111] as follows: firstly, legislation found more problems, while a HR approach will modify the situation. Also, while current rules label the users as deviants, the HR strategy is merciful with them. Additionally, while people use drugs, he found that HR gave a practical and immediate response. He claimed that HR proposed that drug use is non-avoidable, and the problems are caused by laws. He ensured that supply reduction and demand reduction should be supported by society. Moreover, he rejected the merciful concept of HR towards drug users because they harm people and the community, and he preferred that the compassion should be forwarded to the people harmed instead of the drug users who caused the harm. Regarding the point of responsibility of laws to produce more problems according to HR advocates, he claimed that HR tried to put the responsibility of problems on non-users such as the drug industry and the rest of society. Another point is the ignorance of HR proponents that drug use changed with social agreement and access to drugs. In the same way of a prevention approach to tobacco, or to

drinking and driving, it is better not to start using drugs. Finally, he reported what was published from independent networks about the inability of HR to reduce some problems related to drug abuse, e.g. production, drug tourism, and few “needle and coffee houses” programs [111].

8.1.4 A focused overview of HR evidence

One of the studies that discussed the evidence behind the HR approach was the Haydon and Fischer study [10]. They published the necessity of a systematic evolution of a “crack-kits program” to establish the evidence of this program and to provide policy makers who are interested in public health with the outcomes. They discussed reports that indicated the increase of crack smoking in Canada, without similar attention being given to crack smokers compared with injecting drugs users (IDU). Only a few studies had focused on the evidence of crack smoking as a hazardous factor to transmit HIV and HCV. The hypothesis behind this is the possibility of the sharing of pipes that might be contaminated with blood from one user to another. Crack smokers usually have cuts and burns in their lips because they use glass or metal pipes with sharp edges, which could be the reason underlying virus transmission.

Ritter and Cameron [104] published a 2006 review about the efficacy and effectiveness of HR intervention that covered various topics such as tobacco, alcohol, and illicit drugs. They said that most of the literature is focused on illicit drugs compared with other practices. HR concerned about alcohol abuse is focused on reducing road trauma, while for tobacco it is focused on new products that decrease the negative effects linked to smoking tobacco. Although, tobacco interventions are still debatable, hopefully they reduce smoking problems. While for interventions with illicit drug users, there is stronger evidence from efficacy, effectiveness, and cost data that were provided from NSPs. However, other routes of administration do not have similar solid evidence through published studies. So wider research is still required to build more evidence about HR interventions to provide the evidence to policymakers who have not yet adopted the cost-effectiveness of HR interventions [104].

8.1.5 Crack literature review

One of the first reports about smoking crack cocaine instead of snorting cocaine hydrochloride was published in 1986 by Washton and co-authors [8]. They mentioned how crack cocaine was prepared from cocaine HCl by dealers who prefer to promote crack cocaine more than cocaine HCl. They attributed this shift from cocaine (salt) powder to crack cocaine to the high addiction effects of crack cocaine that can reach the brain in less than ten seconds. Smoking cocaine was preferred in use for 81% of drug users in the samples that were interviewed [8]. One of the serious findings in their study was the reported quick arising of health problems compared with cocaine (salt) powder. In the case of crack cocaine, drug users reported hazardous drug-related problems in less than six months, while in the case of cocaine (salt) powder, drug users usually reported drug-related problems after two or more years [8]. Nearly a quarter-century later, Fischer and Coghlan [112] referred to crack cocaine use as one of the most harmful phenomena regarding the social and health problems related to drug abuse. Using crack was associated with high rates of poverty, homelessness, and shortage of fundamental support; all of this caused social problems associated with crack use. Mental health problems were the most reported health problems for crack users. Additionally, Fischer and Coghlan [112] compared the crack cocaine interventions with help for other drug users, e.g. needle exchange program (NEP), and programs of opioid maintenance treatment. They stated how the safer crack use kits were not allowed to show their potential effect publicly, and how such help was kept under limited resources, while other drug programs were widespread e.g. NSPs [112].

Going Dutch - a study in Holland

Cohen and Sas interviewed cocaine users and then they followed up the users after four years [113]. After analysing the data following 64 cocaine users, they concluded that there was a reduction of high levels of cocaine use, and stability of low levels of use during the four years of the study. They found that 6% of their follow-up respondents asked for help to control and quit their cocaine use. These findings helped the authors to conclude that avoiding police intervention and distribution on a limited scale of cocaine did not necessarily increase by a huge number cocaine abusers who did not control their consumption. There were only a few respondents

who quitted cocaine completely for different reasons. Negative reasons were mentioned such as physical and mental effects; one reported the cost of cocaine as a reason to stop using cocaine.

The results of this study were collected in 1991 from 64 follow-up respondents out of 162 cocaine users in the first study (1987). They reported [113] that the majority of follow-up respondents had reduced their cocaine consumption either largely or even completely. Some of them had obtained help to decline their cocaine use, even stopping it. They discussed the opinions of respondents about cocaine policy and what they would prefer cocaine policy to be. Indeed, 34 % of the respondents preferred that the cocaine policy should be stricter for many reasons. The most common reasons behind their opinion were the dangerous and addictive effects of cocaine. While other respondents preferred that the cocaine policy should be more liberal and with less police-involvement [113].

Another study in Holland aimed to examine the prevalence of drug use in Amsterdam in the period 1987 - 2001 [114]. Abraham and co-authors collected data from drug users in Amsterdam to study the changes that happened during these 14 years. Regarding cannabis, one of the most prevalent drugs, its use had increased from 23.2 % in 1987 for those who ever used it to 38.1 % in 2001. While cocaine use had increased from 5.7 % to 10 % in that same time-frame [114]. However, the prevalence of drugs was still the most in Amsterdam compared with other cities in Holland. At the same time in 2001, when cannabis use was 38.1 % in Amsterdam it was 22.4 % in Rotterdam. Possible reasons behind the differences could be that Amsterdam is a metropolitan city compared with other cities, or due to drug tourists, or the large number of places selling cannabis in Amsterdam. The researchers were unable to generalise the results from the capital to other cities or areas [114].

Reports from England and Wales

A study about the drugs and chemical poisons involved in deaths in England and Wales was published in 2014 by Handley and Flanagan [115]. They showed the poisons trend between 1993-2011. There were various aims for this: scanning the poisons to help prescribing practices, product-safety, and other legislation about available treatment and medications. Also, it can provide the evolution of the required analytical toxicology procedures and services. The peak of deaths related to cocaine was in 2008, the total number of deaths was 235 cases (Fig. 8.1). This

included death due to: cocaine alone, cocaine with alcohol, and cocaine with other drugs. Measuring cocaine and its metabolites in blood is a confirmatory test; it should not be the only evidence to claim the cause of death [115].

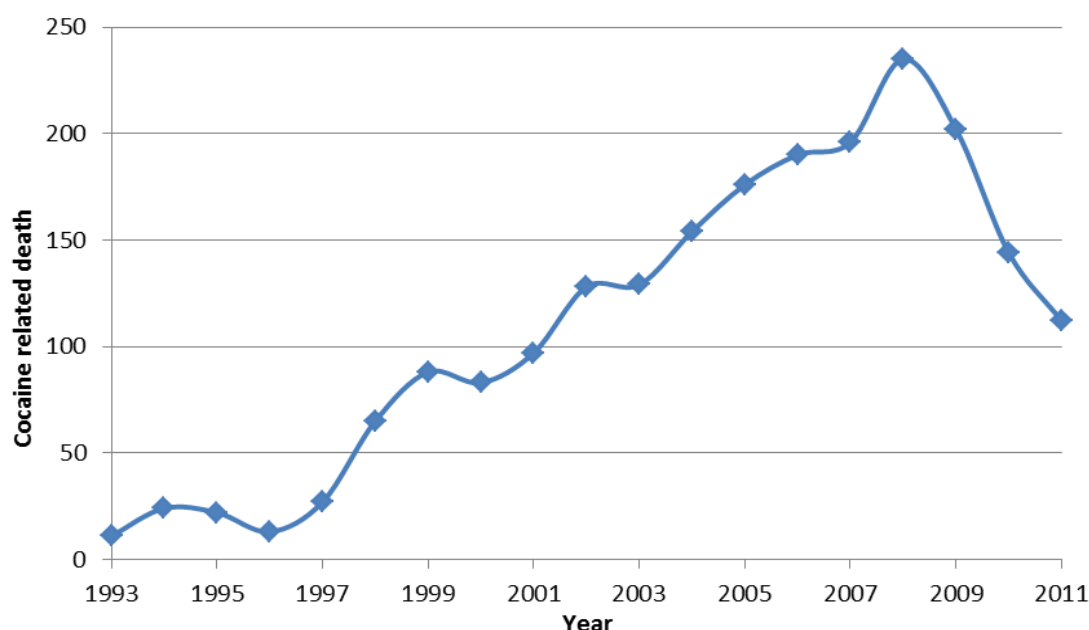


Fig. 8.1. Cocaine related deaths in England and Wales (modified after [115]).

According to a Home Office bulletin in 2012, cocaine was the most seized class A drug [116]. The amount of seized cocaine had decreased between 2010/11 and 2011/12 by 1% to be 17449 seizures, 96 % of those seizures achieved by the Police and the rest by the UKBA [116]. The same record showed that the amount of seized cocaine in 2011/12 was 3.5 tonnes compared with 2.9 tonnes in 2010/11, but it is still gradually decreasing from 6.9 tonnes in the peak at 2003 [116]. The Home Office report the figure for crack separate from cocaine. Crack seizures declined by 8 % in 2011/12 (4971 seizures) compared with 2010/11. The peak was in 2007/08 with 7578 seizures. The total amount of seized crack in 2011/12 was 34 kg, 88 % was seized by the Police [116]. Concerning these data, many studies evaluated and measured the efficiency of HR approaches in UK. The legal HR approaches in the UK include NSP.

CAP Canada project

HR has played a strong role in substance misuse policy in Canada during the last few decades in different interventions, e.g. hostels for homeless alcoholics,

nicotine patches, supervised injection facilities [117]. In the last decade, studies focused on the growing spread of smoking crack cocaine and the problem of sharing crack pipes that could be a route for the transmission of infectious diseases. Also, HR strategies were interested in reducing other associated health problems with the use of some illegal drugs e.g. cannabis by youths. The studies presented that increased health problems for drug users may be accompanied with repeated and chronic use, or unknown contents of drug samples. For that, HR was aimed at raising the preventive education to decrease these problems by concentrating on specific risky behaviours [117].

At the same time as the previous report, Haydon and Fischer [10] reported smoking crack in Canada as a relatively neglected health problem by comparing with the interests and studies of other problems, e.g. IDU. In the case of no available systematic data on the prevalence of crack use in Canada, different studies tried to evaluate the prevalence from their samples of people [10]. A monitoring report in four Canadian cities had found that 52.2 % of IDUs had used crack in the last 6 months, in Toronto 78.7 % of IDUs had smoked crack. Smoking crack is associated with a possible risk factor for HIV, HCV [10, 118], and tuberculosis (TB) via sharing crack pipes through the blood particles that contaminate the device. The sources of those particles are from the sores, burns, and cuts in crack smokers lips which usually need a long time to heal [10, 118]. All of those associated problems with smoking crack were pushing towards designing a unique intervention to distributing 'safer crack use kits'. Safer Crack Use Coalition (SCUC) of Toronto was the first formal network that distributed such kits in Canada. SCUC is a specialised coalition of community agencies and individuals formed in 2000 [10]. The declaration of many agencies and groups that were involved later in the distribution of safer crack use kits was to hamper the transmission of infectious disease that could spread through sharing crack pipes and using harmful materials to make their hand-made crack pipes [10]. Haydon and Fischer [10] also reported the controversy in the political and police decisions towards distributing the crack kits. In Toronto, distributors and users of kits are charged under the Controlled Drugs and Substances Act (CDSA). On the other hand, in Vancouver, a Vancouver Police Department spokesman declared that possessing and producing any components that may be used in smoking crack is not illegal. This contradiction between different areas, and in the media, made some

politicians refuse to give support for this project because the media presented it as a legalisation of drugs [10].

Leonard and co-authors had evaluated the Safer Crack Use Initiative in Ottawa, Canada in 2006 [119]. The evaluation was estimated through recruiting active IDUs who smoked crack. They were interviewed and provided saliva samples for HIV and HCV tests at four time-points. Regarding the results of those interviews, a significant number of IDUs reported a decline in collecting mouth pieces after 6 and after 12 months. The IDUs mentioned that they preferred alternative materials, due to their previous mouth injuries during crack smoking. This behaviour may require further research about using alternative products that should be offered instead. Furthermore, other decreases in brass mesh-screens from the initiative were reported at both times (6 and 12 months). The reason IDUs gave was that they use other metal materials, e.g. Brillo pads or Chore Boy, this metal usually breaks when it is heated which produces dangerous particles. Those particles are inhaled into the mouth or lungs of the smoker causing mouth bleeding or lung damage. These results require further informing and counselling crack smokers about this risky and potentially harmful behaviour. Also, 25 % of crack smokers reported confiscation or ruining of pipes by police which requires more discussion with law enforcement agencies about those cases. Additionally, 25 % of IDUs, after 6 and 12 months, mentioned that they smoked more frequently after the availability of crack kits. Although those results appeared negative as an outcome of the study, this was associated with a significant decline in injecting behaviour, about 50 % of participants reported fewer injections since they had access to safer crack smoking kits. This could therefore be considered as evidence of transforming from injecting, which is a high-risk behaviour, into smoking which is a lower-risk behaviour compared with injecting. One of the most important and significant results reported by Leonard and co-authors [119] was to measure the decline in sharing crack pipes. From more than 33 %, at 6 months before starting the assessment, down to 13 % after 12 months is a continuous positive change in the behaviour of sharing crack pipes. This change requires encouragement and the provision of further support through keeping the service of the Safer Crack Use Initiative going.

Johnson and co-authors explained the lessons of Safer Crack Outreach, Research and Education (SCORE) after three years [120]. The SCORE project contained two main elements: kit-making circles and kit distribution. They used

different methods to collect information and data about the project e.g. pre- and post-survey, qualitative, quantitative, and field notes from kit-making circles, kits distributors, or kit recipients. To understand the outcomes of the project and the limitations, the political changes should be mentioned e.g. the Federal election in 2005 that brought the Conservative party to power when the Prime Minister announced that he did not support HR strategies, and his Government prefers crime control strategies. Also, the 2002 election in Vancouver brought neo-liberals to power that cut off these services, public housing, and community based programmes. Furthermore, the cancelation of the Ottawa program by the City Council in July 2007 was due to a belief that the program increased the use of drugs. However, there are various harms associated with smoking crack, most of them are related to the practices of smoking crack. Using crack pipes which may be split or broken leads to damage to the lips or hands. While using steel wool as meshes can produce metal particles during heating. Such particles cause bleeding in the mouth or respiratory damage. Pipe sharing is a factor in the transmission of HCV and HIV. After one year, there was a change in crack smokers' practices towards safer crack use, but pipe sharing was still reported. Moreover, there was an increase in using items of crack smoking kits. The results of distributing these kits led to a recommendation to increase the counselling and educational services about sharing items and other safer smoking practices [120].

One of the limitations of their report was the lack of availability and the limited distribution of HR workers in the cities. Despite such limitations, the awareness of services provided to crack smokers grew from 28.2 % to 34 %, whereas 43 % of participants did not receive any support before this project. Johnson and his co-authors finalised their report with a few recommendations based on the outcomes after three years of running SCORE. They recommended integrating the distribution of crack smoking kits into other current HR services. The efforts should include various interventions and strategies to continue the education and awareness aims of the project. The educational objective should be comprehensive enough to cover different practises and other marginal groups of drug users. The services should be provided to women and include emotional support to women who use crack under special circumstances. A recommendation of the research was to measure the effectiveness of HR approaches to help drug users to be more safe [120].

8.2 Theories of behaviour change and the Information Motivation Behaviour model (with evidence)

8.2.1 Introduction to theories of behaviour change

A supportive base could add more help in the design of interventions from the theories of behaviour change, but the theories do not have the protocol of how the intervention will be applied. This has increased the importance of theory-based intervention development. With respect to complex interventions, the Medical Research Council (MRC) in the UK has reported an approach to develop and test such complicated interventions. Their approach includes three phases: they start with a theory phase in which the theoretical evidence of the intervention that will be developed in the next phase is collected. The second phase is a modelling phase that provides the hypothesising and evolution of the behavioural factors “What” and the techniques to change the determinants “How”. The experimental phase is a challenging phase for researchers, where they face problems because they may not completely and fully identify and optimise the intervention. Supporting the use of theory in designing interventions has three principal reasons: the first is that the interventions are possibly more effective when behavioural determinants are identified and they depend on knowledge about such determinants. Secondly, measuring and optimising the theory is done by assessing the interventions, through providing the theoretical information about the interventions and evaluations. Finally, the interventions help researchers to understand how the interventions work [121].

The behaviour of drug users could be related to many variables. This shows the complexity of designing an intervention or choosing a theory to explain the behaviour. In this study which is based on information increasing awareness about smoking equipment and impurities, there is more than one theory that contain relevant variables, e.g. knowledge, motivations, behavioural skills. Some relevant theories will be mentioned below, then the chosen model will be discussed as a result of developing previous theories due to the limited results of using only one variable to modify the behaviour of drug users.

8.2.2 Health Belief Model (HBM)

The Health Belief Model (HBM) is the most commonly applied framework in health behaviour studies since the early 1950s [122]. The HBM contains several determinants that predict the reasons for people's behaviour such as why people perform in some way, to avoid or to do tests, or to manage disease conditions. Those determinants contain: susceptibility, seriousness, benefits and barriers to a behaviour, cues to action, and self-efficacy (Fig. 8.2).

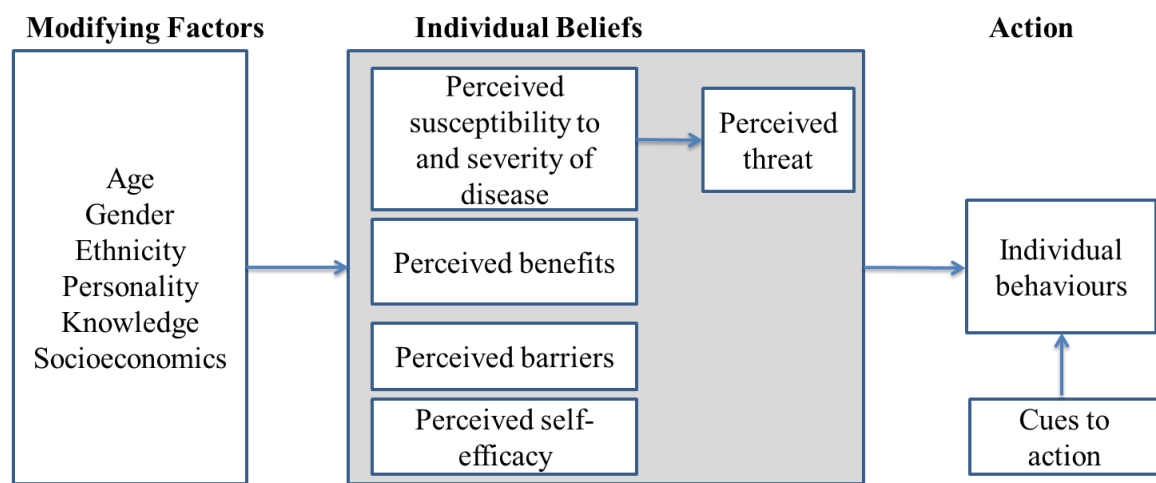


Fig. 8.2. Health Belief Model components and linkages (modified after [122]).

Fig 8.2 shows the individual health beliefs as the major constructors, while the modifying factors that may affect health perception include knowledge and socioeconomic factors [122]. Although the individual beliefs and modifying factors that were determined in the HBM may end in outcome behaviours, the relationships between the factors are still ambiguous and unclear. This may explain the variation between the studies that are based on HBM. Therefore, further analytical strategies are required to determine these linkages for any further prediction behaviours' application of HBM.

8.2.3 Theory of Reasoned Action (TRA) and Theory of Planned Behaviour (TPB)

Theory of Reasoned Action (TRA) and Theory of Planned Behaviour (TPB) both concentrate on the importance of individual motivational elements as factors to practice certain behaviour, and perceived control over the practice of the behaviour.

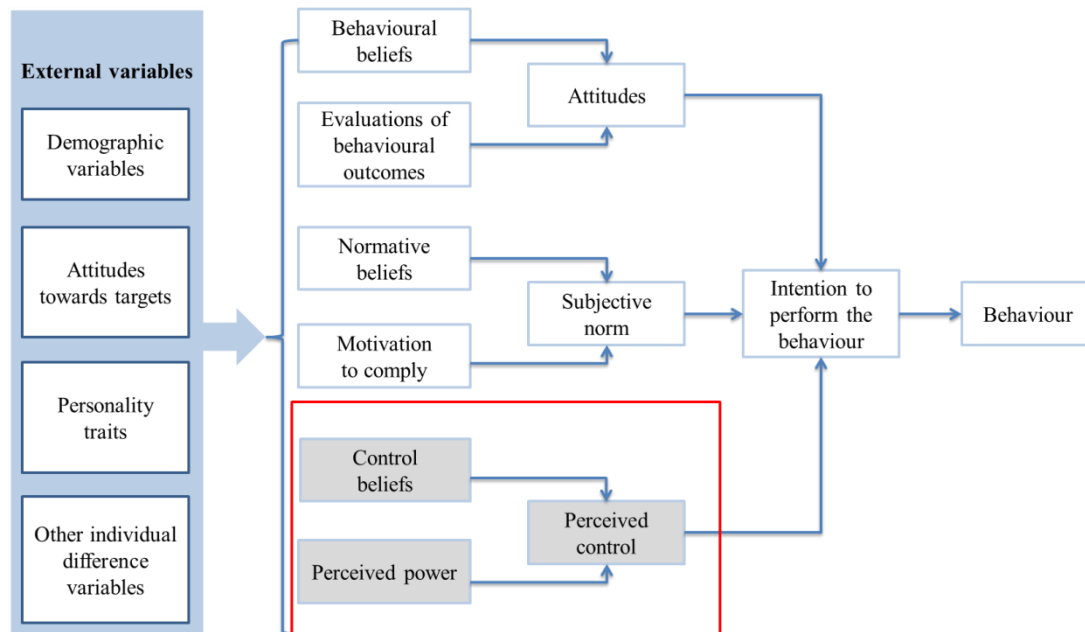


Fig. 8.3. Theory of Reasoned Action (TRA) and Theory of Planned Behaviour (TPB) (the upper light part of the figure represents the constructors of the TRA, while the total figure shows the TPB) (modified after [122]).

Control beliefs and perceived power determine the perceived control over the behaviour. The control beliefs represent the existence or absence of facilitators and obstacles to behavioural practice, also they are supported by perceived power or the effect of each variable to ease or obstruct the behaviour (Fig. 8.3).

The TRA and TPB have the same assumption that attitude toward the behaviour and social normative perceptions determine the behaviour intention which they consider as the main predictor of the behaviour. Moreover, normative beliefs which are the main references for people to agree or to refuse to practice the behaviour, and motivation to comply with those references, determine the subjective norms of people. TRA and TPB theories were successfully used to predict and

interpret several health behaviours and substance abuse, e.g. HIV/STD-prevention behaviours, smoking, alcoholism, use of contraceptives [122].

8.2.4 Social Cognitive Theory (SCT), Social Learning Theory (SLT)

Social Cognitive Theory (SCT), or what was called Social Learning Theory (SLT), was developed on concepts of learning within circumstances of human social environment [122]. Most social and behavioural theories concentrate on the determinants that form individual and group behaviour, while the SCT assumes that the behaviour of humans is the result of the interactive effects of individual, behavioural, and environmental effects. This theory focuses on the environmental effects on human behaviours, but it recognises the abilities of individuals to change and to form the environment to shape suitable purposes. As well, it could encourage interactions between individual capacities and their environments. All of this could enable people to work together. People with different skills can work within an organisation to accomplish altering the environment that ends in bringing benefits to the group. SCT aims at providing a thorough understanding of why and how individuals alter their health behaviours and their social and physical environments. Although SCT has a strong base for designing practical research and practice using various techniques and strategies to change harmful behaviours. To achieve fully an evaluation of the SCT, various SCT concepts require further evaluation through experimental studies, being repeated for different behaviours and populations. The evolution of each element can show the impact of each concept in different behaviours [122].

8.2.5 Information Motivation Behavioural skills (IMB) model

The central elements of IMB are information, motivation, and behavioural skills. The model starts with information. The information element is linked directly with prevention behaviour outcomes [32]. In the case of the HIV prevention model, the information element can include details and tips about HIV transmission and facts related to HIV prevention, this can be used as a guide for preventive practices [123].

The IMB model was one of the models that has been applied to understand the HIV risk behaviour. Theoretical interventions were designed depending on the IMB

model to alter the behaviour across wide groups of populations involved [123]. The IMB model was developed through using psychological theories and methodologies to find the (then urgent) need for HIV/AIDS preventing interventions with a theoretical basis. This model was affected by the work of Fisher in 1988 on the influence of social circumstances on the behaviour of HIV prevention [124].

The idea behind the concept of the IMB model is to try to overtake the limitations of theories in social and health psychology [32]. Some of those limitations that IMB tries to answer are: the absence of particular relations between the principal elements of behaviour prediction, lack of presumed validity of key determinants, and absence of determinants that may have an essential role to understand and alter health related behaviours [32]. Since the first publications about the IMB model, it has been supported with evidence through correlation and experimental intervention research in the field of HIV prevention and other health behaviours [123, 125, 126]. The role of IMB is to develop a tool of the psychological elements of HIV prevention behaviour and to afford a general scheme to find out and to advocate those interventions. Not surprisingly, this model concentrates basically on the group of informational, motivational, and behavioural skills elements which are experimentally and theoretically correlated with HIV prevention [123].

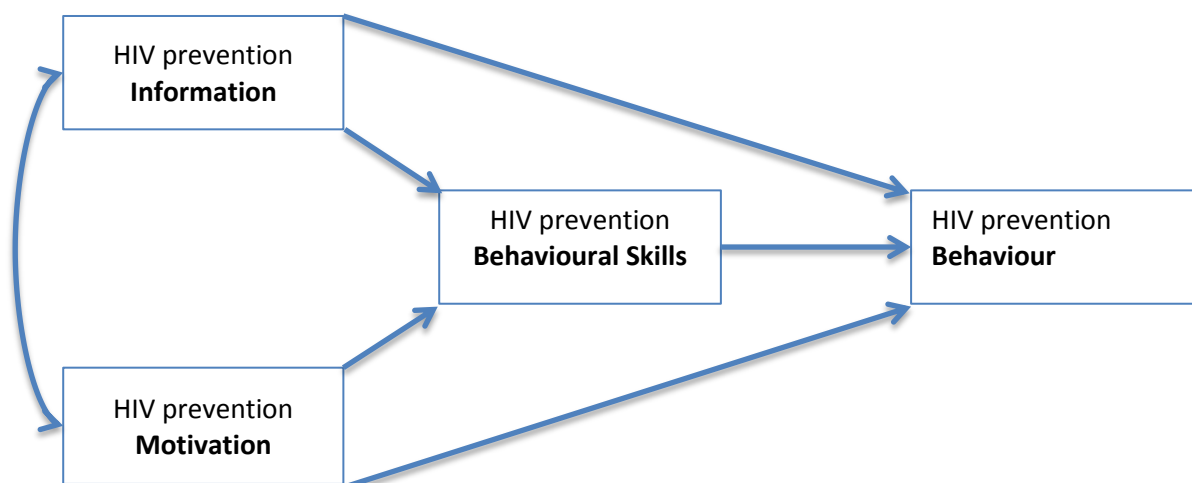


Fig. 8.4. The Information Motivation Behavioural skills model of HIV prevention interventions (modified after [127]).

The second determinant element of the IMB model is motivation which is involved in preventive practices and to measure whether well-informed people could be persuaded to alter their risky behaviour as they were well-informed about risky

behaviour. In the case of HIV prevention intervention based on the IMB model, a motivational determinant can include personal motivation to practice preventive behaviours. Also, it includes social motivation to join in prevention intervention [123].

The third element of the IMB model is the behavioural skills. These are essential for preventive behaviours. They measure if even well-informed and well-motivated people can be capable of performing preventive behaviour efficiently. These behavioural skills consist of the ability of an individual and his/her recognised self-efficacy in accomplishing the series of preventive behaviours that are associated with achieving prevention. In the case of HIV prevention behaviour intervention, behavioural skills can contain objective and recognised abilities, e.g. to buy and use condoms, to discuss regularly condom use during sexual intercourse, the ability to build-up the self and the partner for continuous types of preventive behaviour practices over time, among other similar behaviours [123]. Fig. 8.4 shows how the preventive information and preventive motivation can act initially through the behavioural skills to effect prevention behaviour [123, 127].

In the case of HIV prevention intervention, from the first studies in using the IMB model, Fisher and co-workers used a model to test experimentally the relationships between IMB model elements. In their samples of heterosexual university students [128], the prevention information and prevention motivation were statistically independent elements. Prevention information and prevention motivation were separately related with prevention behavioural skills. Prevention behavioural skills were connected with prevention behaviour by itself. Also, an explicit relationship was observed between prevention information and prevention behaviour, as well as between prevention motivation and prevention behaviour [128]. These findings were confirmed by other studies for male Indian truck drivers and women with low income who are also sex-workers [126, 129].

Another example that applied the IMB model was in expecting Breast Self-Examination (BSE) and relevant behaviours in women [130]. This study broadened the application of the model beyond prevention behaviours related to HIV-related behaviours. Models of behaviour change were used to design a framework to explore the reasons behind the achieving (or not) of BSE. However, some studies had suggested that lack of knowledge and practice of BSE could be the reasons of low levels of BSE, while others reported embarrassment as a negative feeling (anti-BSE

attitudes). One of the other reasons which correlated significantly with BSE performance was levels of perceived normative support by women. The negative attitudes to BSE and the modest perceived normative support could result in low intentions to practice BSE which may be recognised as a lack of motivation. Moreover, women might be suffering from lack of behavioural skills required to test their breasts effectively [130].

On the other hand, one of the limitations of the IMB model is the role of the information element to predict prevention behaviour. The disagreement about the role of the information element in behaviour prediction made it a conflicting contributor [123]. The reason behind this inconsistency in a role for information could be the presumed knowledge of participants in some studies which may affect such a contribution. Another question is the relation between prevention information and prevention motivation, where some studies showed that they are independent and some that they are not. The models explain that well-informed participants are not necessarily well-motivated and vice versa [123].

The behaviour theories present different theories which try to explain the behaviour determinants. The IMB model may collect different elements that cover more than one theory due to the complexity of interactions between behaviour determinants. Previous studies and projects for crack smoking and drug users focused on providing kits to reduce the health associated problems. In this study, the intervention is based on the idea of designing an intervention to inform crack smokers about the purity, pipes efficiency, and HR tips about smoking crack. This intervention will be the first attempt that will use laboratory results of profiling seized crack samples to design an educational intervention. The intervention will be based on analytical results from experiments that used crack samples to quantify cocaine base, cutting agents, and smoking crack model results that present differences between common smoking equipment and the associated health problems. Also, HR tips about health problems related to smoking crack will be offered. The educational intervention aims to inform crack smokers and raise their awareness about their smoking behaviours to encourage them to reduce risky habits and choose any alternative to avoid those problems. Indeed, this intervention will be the first tool that drug workers can use to communicate with crack smokers because currently there is no treatment or supplied paraphernalia for them. The HR workers will participate in focus group interviews to discuss the intervention and how it could be optimised.

Chapter 9

Methodology and Methods

9.1 Methodology

The aims for pharmacy practice/social science research studies require methods for collecting and then analysing the collected data, interpreting the results, and reporting the data. There are many procedures for achieving the research aims, and these models have different names. Precise research design is critical for the studies to enable researchers to make decisions, so they must design the methods that lead them to discuss their results logically. One of those methods is called mixed methods which concentrates on carrying out qualitative and quantitative experiments in one or more studies. This means that the phases include collecting, analysing, and then interpreting data for both the qualitative and quantitative experiments. The central aim of using mixed methods is to combine both data sets and then to apply them to obtain a better understanding of the study question than that gained using only one approach. The need for these kinds of methods is both the strength and weakness of each approach. The quantitative approach provides data that can be generalised because the data are collected from large sample sizes. However, the qualitative approach uses a smaller sample compared with the quantitative approach and provides details and in depth data that can answer some questions which analysis of quantitative data alone cannot [131]. In practice, there are also other reasons to use mixed methods. One approach provides data that may not be enough, or the collected data require further interpretation which requires collecting more data using another approach. Furthermore, a second approach could be required to improve the first approach, e.g. the qualitative method can provide individuals' prospective about the research that can yield a better understanding of the quantitative experimental results. Such a study will incorporate a series of phases [131, 132].

Carrying out the mixed methods approach has different procedures that may look similar at some steps and different at others. The main characteristic steps to use in mixed methods research design are: collection and analysis steps include both sets of qualitative and quantitative data, then mixing both data sets in different ways and at different times or levels. The application of this research method can be achieved for

both approaches at the same level of priority, or priority could be given to one approach more than to another. Generally, mixed methods can be a single separate study or a part of a series of study phases [132].

There are many types of classification and identification of mixed methods approaches that could be applied in this research. The four main types of mixed methods are: the triangulation design, the explanatory design, the exploratory design, and the embedded design. The triangulation design is one of the most familiar and well-known designs which aims at collecting various but complementary data at the same time from qualitative and quantitative methods to enhance the understanding of the research problem. Regarding the process to implement the triangulation method, it is a single step where researchers carry out both qualitative and quantitative experiments at the same time and with equal priority.

Secondly, the explanatory design consists of two design phases. It starts with quantitative experiments, then the quantitative results are explained by carrying out qualitative experiments. It is used for different purposes, e.g. to interpret significant or surprising results. There are two different models included in explanatory design: the follow-up explanation model and the participant selection model. Although both have quantitative data then followed with qualitative data, they have differences in the priority of each phase and the connection between the phases. The first one focuses more on the quantitative results while the second is concentrated more on the selection process of participants and the qualitative phase of the method. Thirdly, the exploratory design also has two design phases. The results of the qualitative method (the first phase) could help to enhance and inform the quantitative phase (the second phase). There are some assumptions behind this design: only limited parameters for quantitative design are available, but nothing accurately representative of this study, the variables for the quantitative phase are unidentified.

Finally, the embedded design also consists of two design phases, where one has a secondary and assistant role to the main data type on which the study is based. The assumptions of this mixture are that one data type cannot provide enough data to answer the study questions, therefore requiring other data types to complete the answers. This type of design is usually applied in experimental or correlation studies when researchers want to enhance treatment procedures, to test the mechanism of an intervention or related variables, or to follow-up on the outcome of the experiments.

There are various procedures available to carry out the research study. The research can embed the qualitative data with the quantitative method at different levels that can be achieved in experimental design (Fig. 9.1). Also, the quantitative data could be embedded within the qualitative method which could be in the correlational design. The experimental design could be considered as the most common design of mixed embedded design. Fig. 9.1 shows that the priority in this model is mainly quantitative data, while the qualitative method has a supportive role at different levels. The embedded experimental design could be performed in two types: the qualitative data could be embedded before the intervention to enhance the treatment procedure or it could be embedded after the intervention to interpret the treatment's outcomes.

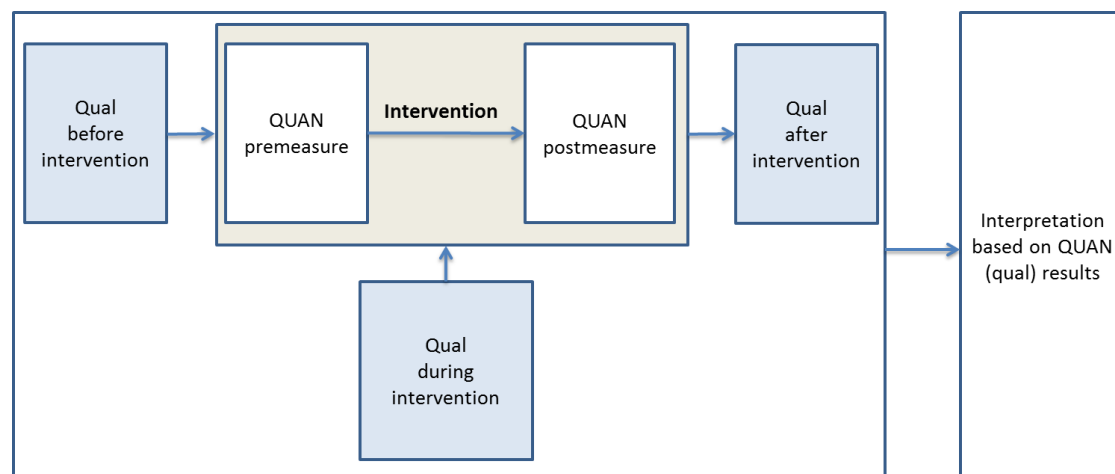


Fig. 9.1. Embedded design: embedded experimental model (modified after [133]).

An example of embedded mixed methods is that of Messer and co-authors in their study of the early detection of cervical cancer among Native American women, with participants from two tribes in North Carolina. The primary quantitative analysis of the intervention found moderate outcomes and different responses between the two tribes. The design of qualitative methods was to provide quantitative data with support about the assessment of an educational intervention for the early detection of cervical cancer (Fig. 9.2). The varied outcomes between the groups in quantitative outcomes were not expected by the researchers, and the collected data in the quantitative phase were not enough to interpret the variations. Therefore, a qualitative complementary analysis was run. They found some factors influenced the intervention outcomes. The role of the qualitative phase was to collect more data

about how and why the intervention was or was not effective, to provide the identification of factors modulating the intervention results, and to give sensitivity to the program by using the results within its social, cultural, and historical environment [134].

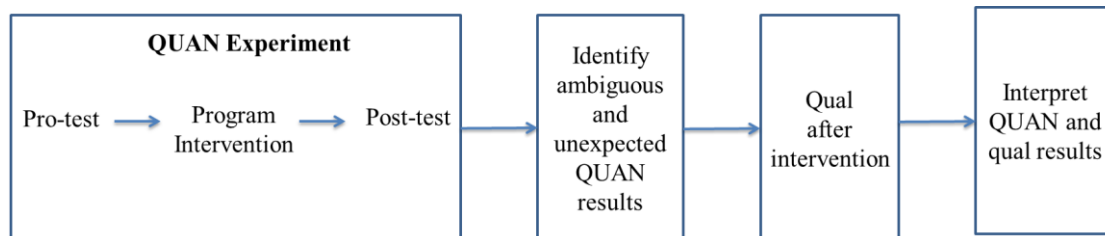


Fig. 9.2. Embedded design: Messer's embedded design (modified after [134]).

In this study, the crack smokers will participate in the quantitative part to present their knowledge and behavioural skills of smoking crack. Then the HR workers who delivered the questionnaire and the intervention will attend focus group sessions to give feedback about the questionnaire, and the intervention design, information, and smokers' interaction with these kinds of HR tools. Both parts could give an idea about the crack smokers' knowledge, skills, whether they were interested in educational HR tools, and how we can optimise and use interventions in other drug services in the future.

9.2 Methods

This study was based on more than one research method to address the various issues mentioned in the objectives and to achieve the aims. Three different research methods were applied, i.e. questionnaire, focus group, and telephone interview. They are described in detail in this chapter.

9.2.1 Mixed methods

The purpose of the study is to evaluate the impact of data analysing street crack samples on the behaviour of users. To achieve this aim, HR workers will be engaged who are used to communicating with crack users and who provide drug users with

information and services that may decrease the health problems which accompany the use of illicit drugs. HR workers delivered the intervention and then attended either a focus group or an interview to collect the feedback about the intervention, crack users' interactions with the intervention, and recommendations to develop this type of HR approach.

Mixed methods are chosen in this study to obtain a more complete analysis by utilizing both quantitative and qualitative methods, in order to get a better understanding of the research question by mixing the data sets. The quantitative part was represented by crack smokers who answered the questionnaires both before the intervention and afterwards to obtain a larger sample, and therefore possibly to be able to generalise the results. The qualitative part was conducted by interviewing the HR workers who delivered the intervention and questionnaire in the first step through a focus group or phone interview. The interviews could provide deeper information and better explanations for the crack smokers' behaviours and the effects of the intervention.

9.2.1.1 Quantitative methods

The study included two groups of crack smokers. The first was in Nottingham, while the second used Bristol ROAD (Recovery Orientated Alcohol & Drugs Service) located in Bristol, UK. Bristol ROAD is a provider of services for people who want help due to problems related to drugs and alcohol. These services are delivered by many providers e.g. Bristol Drug Project (BDP), St Mungo's, Bristol Specialist Drug and Alcohol Service (BSDAS), Developing Health and Independence (formerly known as the Drugs and Homeless Initiative) (DHI), and Addiction Recovery Agency (ARA). There are several services provided in Bristol ROAD for people to help them achieve positive changes in their lives. These services could cover the main pathways that may make people suffer discrimination e.g. accommodation, alcohol, attitudes, thinking and behaviour, children and families, drugs, education, training and employment, finance, benefit and debt, mental and physical health, women subject to domestic abuse, and sex workers.

In June and July 2014, 7 crack smokers in Nottingham, UK and 20 crack smokers in BDP, Bristol, UK were recruited in this study. They have to have smoked crack before to be eligible to be involved in the study, regardless of if they use other

drugs or not, to ensure they have experience about the topic of the study. They had access to traditional services for injecting drugs and substitution treatment for heroin and other drugs. Drug users were individually approached and asked whether they smoked crack and if they were interested in participating in this study. They were at least 18 years old. Unfortunately, there is no available treatment for crack cocaine addiction at the moment. For any help at all, users usually visit drug service centres to get advice or treatment for using other drugs. Due to this lack of any treatment, it is difficult to conduct a study where it is not easy to recruit the targeted participants. All participants were told that the study, entitled “Translating laboratory evidence on the safety of crack cocaine into a HR intervention for use by HR workers”, involved individually completing two questionnaires about their crack smoking behaviour and participating in a single-session about delivering the intervention.

The quantitative part of the study is designed for pre- and post-longitudinal study. The first measure was conducted before delivering the intervention by HR workers, and then the second measure (follow-up stage) was after four weeks in the BDP group, while it was after two weeks in the Nottingham group. All participants continued in the study and they answered the questions in the follow-up stage. They were compensated by vouchers (£15) for each time they attended the session (twice in total). The study protocol was approved by the Research Ethics Approval Committee for Health (REACH) at the University of Bath.

The study started by developing a questionnaire to measure the knowledge, motivation, crack cocaine using skills and habits, based on a previous questionnaire of Cohen and Sas [113], and using the Information Motivation Behaviour (IMB) model for a similar application [129]. The questions had been previously discussed with HR workers in Bristol ROAD to optimise the questionnaire and to avoid any misleading questions or ambiguous words that may be incorrectly interpreted by crack users. Then the HR workers in Bristol and Nottingham delivered the intervention to crack users. The HR workers had also helped to optimise the intervention and gave useful comments through their experience about presenting the information and wording it in simple language.

The optimised questions were focussed on:

1. their history of crack smoking and injecting, their age at first use and with whom it was. This could show the pattern of use and the preferred route of administration to obtain advantages from it or to avoid disadvantages of other routes;

2. advantages and disadvantages of both smoking and injecting crack cocaine. This could provide information that may help to explain desired behaviours and some problems that crack users try to avoid by choosing various routes of administration;
3. source of crack users' drug information. This could show users' prior knowledge and from where they get their information that later determines their behavioural skills. Also, it could show any possible effects of friends, family, and social service workers on their behaviours;
4. cutting agents effect on health, and what cutting agents they expect to be found in their crack samples. This may reflect if there is any impact of the media and the users' knowledge or perception of cutting agents effects. It is not enough to find out whether they know that cutting agents are dangerous or not, but to probe more and ask them about any expected cutting agents that can possibly cause dangerous problems;
5. types of pipes and equipment they use to smoke crack; reasons to choose a specific pipe. This could provide information about desired and disliked effects of using specific tools and how it is possible to avoid the latter;
6. awareness of crack smokers about the quality of samples and whether they check when they buy. This may yield the information that crack users look for and what makes them stop buying samples. This could be based on knowledge or trust in drug dealers;
7. the services in which the users may already be involved. This is to measure if they are involved in other services and whether they are aware of how to get treatment and services related to the drugs they use. This can measure the motivation and awareness about health, and whether the crack users seek treatment and other accessible services;
8. demographic information.

A mixture of closed and open questions was used to obtain the desired information. Closed questions were used to collect information answering either on a scale or using listed choices. Open-ended questions were kept at a minimum level in order to make the questions simple so that they could be answered and completed in only a short time. This type of question was used to add some exploration and to elicit more detailed information than was given in reply to closed questions. The language used was deliberately kept simple to ensure it was clear to people with different levels of education. This could help to find out the exact answer that the users actually mean. The participants were encouraged to provide a good response rate by emphasising that the questionnaire was both confidential and anonymous.

This could ensure that crack users would be honest in their answers and also to avoid any significant fear of being arrested by the Police [135].

Reliability is the extent that a test outcome is the same for the same questions with the same participants at different time intervals. Here it was not suitable to re-ask the same questions for the same participants, as this may cause resistance in the participants. To avoid this resistance, different reliability approaches could be used to test the reliability of the questionnaire. This was assessed through internal consistency which means the extent to which similar questions gave consistent answers, by comparing a reversed question to identify whether the answers to those questions were coherent.

The results of the questionnaire were set up in a Statistical Package for Social Sciences 'IBM SPSS Statistics 20' (IBM SPSS, 2012) and data entry was done by Mohammad Zaher Shehab (MZS). Data entry were checked for all questionnaires (27 samples). Frequency and average test were used to compare two groups, but in general other results were presented descriptively to show the distribution of answers. This study was a pilot to investigate the possibility of transferring knowledge between the science fields. The limited numbers of participants in both groups (<30) prevented further statistical tests, comparing in depth the results from the two different sources.

The PIPES intervention was a translation of analytical laboratory data to inform crack smokers about: purity, cutting agents, hazardous effects of common cutting agents, differences of emitted dose of cocaine between different pipes, health problems associated with various pipes, and HR tips. The main focus in the intervention was to present the results of model crack smoking experiments. This was the main point relating specifically to crack smokers more than to other drugs users or cocaine users who use other routes of administration, e.g. injecting or snorting.

The message in the first part is to use the results to show the difference between pipes' efficiency. It showed that drinks cans waste about two thirds of each sample, and the use of cans is associated with dangerous infectious diseases that can be transmitted when cans are shared between smokers. Other messages included the content of the crack reference sample that was used in a crack smoking model as a reference to conduct all experiments. This sample showed that cocaine is less than 50 % of the sample and phenacetin is the main cutting agent besides a small part of unknown content. Health information focused on the harmful health consequences of

unknowingly using phenacetin. The HR tips concluded the main HR advice for crack smokers, e.g. to avoid sharing pipes, to avoid drinking alcohol when smoking crack, to take a break during smoking, and to drink more water.

The follow-up stage for this part was conducted after four weeks for the BDP group and after two weeks for the Nottingham group. The participants in the BDP group were asked direct questions about their smoking frequency, what type of pipe they used during the interval after the intervention, whether they changed the pipe, if they shared the information with others, and what did they share? The participants in the BDP group were also asked specific questions related to how they spent the voucher which was provided to them after the first session. The participants in the Nottingham group were asked the same questions that they were asked in the baseline session as well as some questions related to the intervention's impact.

9.2.1.2 Qualitative methods

In addition to a first step of quantitative data collection, it was preferred to get further deeper information to provide some comprehension of the impact of the intervention on crack smokers knowledge, motivation, and behavioural skills. The aim of conducting qualitative analysis is to make easier the complete exploration and understanding of the studied phenomena. It could provide answers related to specific questions about the efficiency of using an intervention based on pharmaceutical analysis to inform crack smokers and encourage them to reduce harmful behaviours.

The targeted group for the qualitative analysis in this study was HR workers who provide drug users with different services and treatment. These workers have good relations with drug users enabling them to discuss without embarrassment or fear of being in an illegal situation. HR workers generally supply various types of services, and support not only drug users and alcoholics, but also they provide services related to housing, financial problems, children and family, education, training and employment. The workers involved in this study were working in a HR team. This team focuses on supplying several services, e.g. needle exchange, non-judgemental advice, sexual health advice, condoms, and nursing service. This team visits different places in Bristol to have contact with various drug users. The principal statement of BDP summarises the roles of their activities aimed at reducing harms, promoting change, challenging discrimination, and increasing people's capabilities.

In the Bristol group, two HR workers were involved in the study. They attended a focus group to discuss the intervention, how crack users deal with it, and how the intervention could be developed and supplied to other crack users. Also, the HR worker in Nottingham was interviewed via telephone. The semi-structured interview was conducted in the BDP centre in Bristol by MZS as interviewer and with Dr J. Scott as facilitator. The interview lasted 40 minutes, was audio-taped, and then it was transcribed. In the Nottingham group, the HR worker who delivered the intervention to participants was interviewed in a 20 min telephone call (July 2014). The call was audio-taped and transcribed. It was used to identify the feedback about the intervention information, response of participants, and for recommendations to develop further HR tools. The guidance for the interviews was optimised to extract the HR workers' experience and feedback about the intervention in utilizing this approach with crack smokers through both structured and open-ended questions. The questions include:

1. the impact of information about the emitted cocaine dose via different devices and the health consequences of using different pipes. The design and development of a crack smoking model could be a mimic for the real case of crack smoking. This may encourage users to feel involved in the study, discuss the results, and be more aware about their behavioural skills and knowledge;
2. the purity of street seized crack samples and the effects of phenacetin as principal cutting agent, because present laboratory results about cutting agents could make crack users more curious and motivated to know more about the substances they usually use. Although drug dealers may try to keep their clients safe to keep selling to them, the results show that cutting agents usually have negative pharmacological effects i.e. are toxic;
3. informing crack users with HR tips about how HR could help users to avoid some deleterious consequences and improve their skills to reduce associated harms;
4. efficiency of HR tools and whether they could be effective;
5. HR workers' recommendations to optimise the PIPES intervention and to provide further information and interventions to improve crack users knowledge and skills to encourage them to change their behaviours.

These topics were discussed with HR workers to gain detailed information which was not possible in the questionnaires. The interviews were conducted by MZS and Dr J. Scott was the facilitator in the focus group.

The deductive content analysis was used as a qualitative approach to use the previous elements and knowledge from the questionnaire answers and the IMB model to provide the framework of the model with a valid and extended perspective [136]. All comments on a relevant theme were collected and analysed together. Further analysis could be conducted depending upon the positive or negative attitude towards the responses and the involvement of the participants.

An administrative assistant transcribed the focus group and telephone interview. The author read the transcript to ensure the accuracy of transcription, and clarified the words that were not accurately transcribed by the transcriber. Especially for the telephone interview, where the voice was not always clear. The transcripts were iteratively coded. The codes and themes were extracted from the transcripts and were linked with the results of the quantitative analysis part of the study (the questionnaires). Each transcript was coded by reading it and allocating the appropriate code. To ensure consistent coding, both researchers coded the interviews. Di-coding could produce over-coding for some comments which is preferred rather than to miss any important codes. Codes were determined according to the headings found by the two researchers. The analysis was conducted with MZS and the analysed interview by Dr J. Scott was referred to in the discussion when relevant.

The following materials (set out in Appendix 1) were therefore designed and developed:

1. The protocol of the study was submitted to the Community Board of the University of Bath in order to get the approval for this study. The protocol contained a summary of the project, literature review for the project, aims and objectives, methods, details related to confidentiality, data storage and handling, and online project plan.
2. Ethical approval of the Research Ethics Approval Committee for Health (REACH) at the University of Bath.
3. The baseline questionnaire.
4. The follow-up questionnaire.
5. The PIPES intervention.
6. Guideline to deliver the intervention to crack smokers.

Chapter 10

Quantitative and Qualitative Studies

10.1 Results and Discussion of Quantitative data analysis

10.1.1 Results of Quantitative part (baseline and follow-up, two groups)

10.1.1.1 Demographics

Seven crack cocaine smokers were involved in this first group study (N07), 6/7 male and 1/7 female. They are from the Nottingham area, and their average age was 44 ± 5 years. Their ages varied between 34-51 years, with an average length of crack use of 16 ± 4 years. The average age of first use of crack was 26 ± 7 years (Table 10.1). Three out of seven finished their schooling at 16 or less, while another 3/7 finished between 17 and 18 years old. All the participants in this group are white British.

Table 10.1

Descriptive data of the Nottingham group (N07).

| | Age (years) | Age at first use of crack (years) | Length of using crack cocaine (years) |
|----------------|----------------|--------------------------------------|--|
| Mean | 44 | 26 | 16 |
| Std. Deviation | 5 | 7 | 4 |
| Minimum | 34 | 18 | 10 |
| Maximum | 51 | 35 | 21 |

The second group comprised 20 drug users in the Bristol Drug Project (BDP) from the Bristol area (B20), 14/20 male and 6/20 female. Their average age was 39 ± 8 years, varying between 22–55 years. Their average length of using crack was 17 ± 7 years. The average of crack smokers' age at first use was 22 ± 5 years (Table 10.2). Fifteen out of 20 finished their schooling at 16 or less, while 1/20 finished at 17 or 18 years old, and 4/20 finished their studies at age of 19 years old or more. Fifteen out of 20 participants from B20 were white British, while there were also three white, one Jamaican, and one Indian. All the participants who started the study completed to the

end in both groups. Only 1/20 in B20 did not answer the age at the first use, this question was a validation question, and the participant may have thought that he had answered the question before.

Table 10.2

Descriptive data of the BDP group (B20).

| | | Age (years) | Age at first use of crack (years) | Length of using crack cocaine (years) |
|----------------|---------|----------------|--------------------------------------|--|
| N | Valid | 20 | 19 | 20 |
| | Missing | 0 | 1 | 0 |
| Mean | | 39 | 22 | 17 |
| Std. Deviation | | 8 | 5 | 7 |
| Minimum | | 22 | 13 | 3 |
| Maximum | | 55 | 30 | 28 |

10.1.1.2 Crack use

N07 users mainly smoked crack. Five out of 7 of the participants used to smoke crack between 2-6 times a week, one mentioned that he smokes once a week, and one smokes once every two weeks. In comparison, in B20, the most mentioned pattern of crack consumption is 2-6 times a week. Nine out of 20 reported the same norm of crack use in N07. The second pattern of crack use is weekly with 5/20 compared with 1/7 in N07. Other different patterns of using crack cocaine are reported in this group, e.g. once a day, fortnightly, and less than once a month (Fig. 10.1).

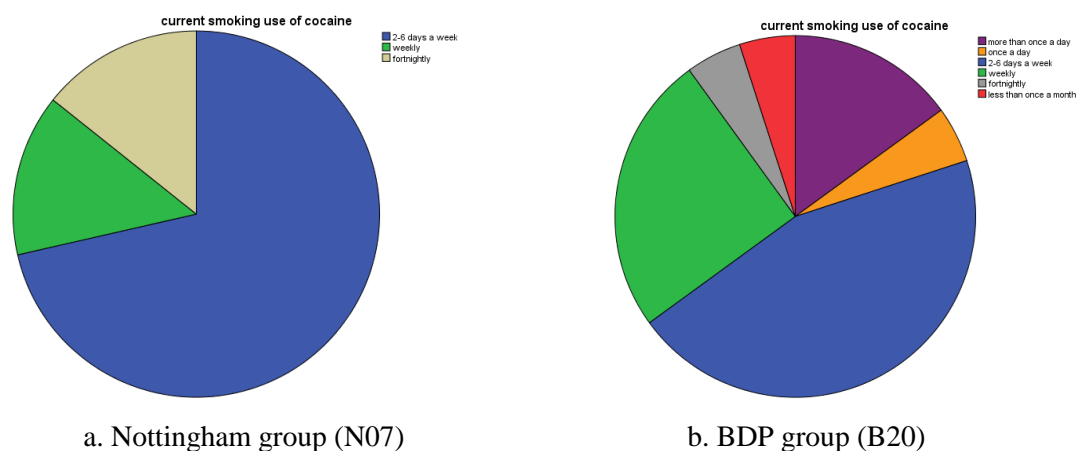


Fig. 10.1. Crack use patterns in the Nottingham (N07) and BDP (B20) groups (baseline).

Regarding the responses towards the choice of crack use (mis-use) method, different opinions showed the diversity behind this behaviour. Some participants used to administer crack by both injection and smoking. In N07, 2/7 said that they only smoked crack. One mentioned that he will inject when he is indoors, while he smokes when he is outdoors. The reason behind this behaviour maybe the preparation steps that he needs in the case of injection and a safe place to do that, while in the street he can find a can or bottle and use it once to smoke a rock of crack regardless of the problems of taking stuff from the street and using it in hidden places far away from the police in order to avoid arrest.

In comparison, in B20 the responses of the choice of crack use method, three mentioned that they only smoke, and two other users mentioned that the route of administration depends on their heroin possession. If they have heroin, they will inject in a combination with crack, while they will smoke the crack if they have crack only. This can refer to the common use of a combination of crack and heroin to get both the effects of crack cocaine as a stimulant and the effects of heroin. This combination is known as “speedball” and may be used to increase the effects of both illicit drugs especially as the effects of heroin last longer than crack to ease the come down [137]. One other reason is the fast route of delivering the cocaine to the blood. The participant from B20 reported that he wanted the crack to be in his body. For that, some crack users preferred either smoking or injecting crack due to the quick peak level of the drug in the blood.

10.1.1.3 Advantages and disadvantages of smoking versus injecting crack cocaine

Related to advantages and disadvantages of injecting crack, according to B20 users, 5/20 who inject crack agreed that injecting crack gives them a better and more immediate hit that they want, faster than smoking crack, while this contradicts the results published by Volkow [138] that found smoking crack reached the peak faster than injecting and snorting. The results were explained as a role of the route of crack administration not to the efficacy of cocaine to block dopamine transporters. This highlighted the fast delivery of cocaine to brain via the inhalation route to reinforce its effects [138]. One of those five added that injecting cocaine is value for money because smoking crack takes all the money he had. Two participants did not inject due to negative issues related to injecting, e.g. vein damage, abscesses. All the crack

users also agreed about the disadvantages of injecting crack cocaine. They all mentioned the health effects, e.g. messing-up veins, BBV, abscesses. This could indicate the level of awareness of crack users towards the negative impact of injecting illicit drugs. This could provide evidence about the importance of health issues for drug users and an impact of informing users about any negative effects associated with their behaviours.

In N07, 5/7 mentioned harmful health issues, e.g. less damage to health, no injection related harms, that could be avoided when they smoke, and that they suffered from them when they inject. Also, 1/7 reported the fast effect of smoking crack compared to injecting it [138], while one mentioned that crack enhanced his down feelings. This agrees with what was published by Falck and co-authors about the association between crack smoking and depression [139]. At the same time, the participants gave varied disadvantages of smoking crack. Two of them mentioned breathing problems due to smoking and using ash such as the chest pain symptoms. The chest pain reported could be explained by the non-cardiogenic effects of cocaine. It could cause alveolar membrane damage or pulmonary oedema [140]. While the other three commented on the size of the effects of the hit and that it is not enough compared with injecting crack. Other comments included “smoking crack takes all the money he has” and “it causes addiction”.

In B20, the crack users mentioned nearly the same advantages of smoking crack cocaine, e.g. rush, buzz, and chasing a high. They also mentioned more and varied disadvantages of smoking crack, as well as breathing problems. They reported paranoia and also ash problems that stuck in the mouth and caused sore throats. Participants in B20 also reported further problems associated with smoking crack, e.g. losing money, involved in violent activities, and committing crimes.

Concerning the users’ opinions in B20 about advantages and disadvantages of injecting crack cocaine, they generally agree with the N07 users about the quicker and more intense effects of injecting comparing with smoking crack. The B20 users also mention the same problems associated with injecting crack: damaging veins, abscesses, and skin problems. Also, they report the risks of getting HCV, and track marks from injecting crack.

10.1.1.4 The first experience of using crack cocaine

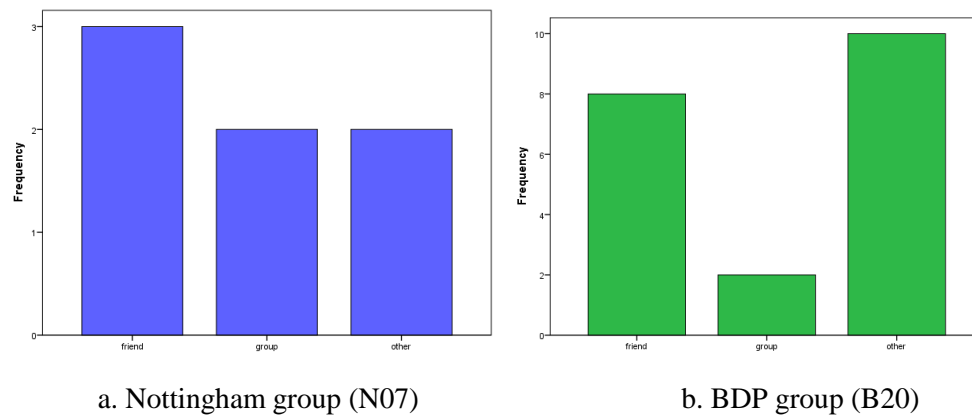


Fig. 10.2. With whom the participants used crack cocaine first time.

In N07, the data revealed that nearly half of the participants (3/7) started using crack with friends. In B20, 8/20 reported that their first use of crack was with a friend. Only 2/20 in B20 started within a group of smokers. The rest had a different companion for their first crack use experience. They mentioned that they started either with another user, drug dealer, ex-partner, or boyfriend. In B20, some mentioned partner or boyfriend as the first person with whom they used crack (Fig. 10.2).

The first place of using crack was mentioned by 3/7 of participants as in their own home and 2/7 in their friends' houses. This can be due to the need for safety and privacy by users to practice their behaviours. Most users did not prefer, for the first time at least, to share the experience with others, compared with some users who mentioned that they tried crack cocaine for the first time either in a crack house or in a youth club with other people (Fig. 10.3).

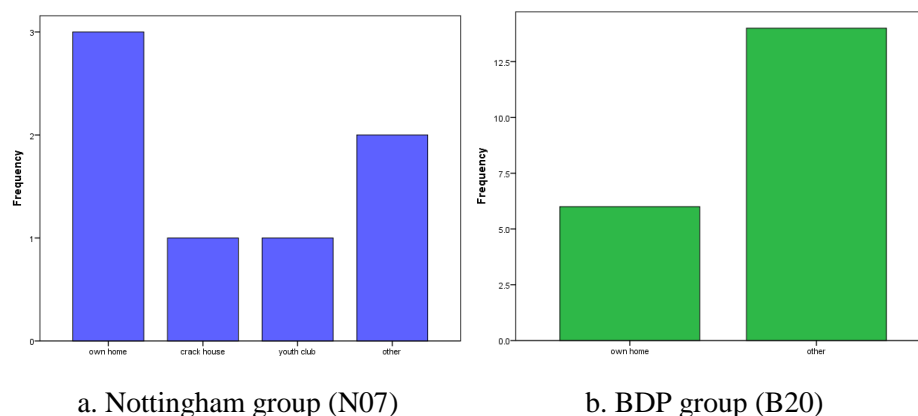


Fig. 10.3. The place of first use of crack cocaine.

Related to the crack source, nearly all users 6/7 in N07 reported that they buy their crack, while only one mentioned that he either washed it up or he was given it. Washing-up being a technical term for recovering spent traces of crack. On the other hand in B20, the source of crack cocaine for 18/20 is buying, while only 2/20 reported that they were given it. In B20, no one said that he washed-up the crack compared with the 1/7 in N07 who said that.

10.1.1.5 Use of crack pipes

The use of various pipes was reported. These pipes included the pipes made to smoke drugs, e.g. stem pipe, ball pipe, or other handmade tools used to smoke crack, e.g. cans, inhalers, glass bottles. There are many reasons behind the use of each one. In N07, all participants reported the pipes they used commonly. The stem pipe was mentioned by 3/7, while the ball was mentioned by only 2/7. Regarding handmade equipment, cans were reported by four smokers to be used as the smoking device. The medical inhaler was mentioned 3 times, and glass bottles were mentioned only once. In B20, none of the 20 participants reported that they used a stem pipe. Only 2/20 reported that they used ball pipes, also 2/20 mentioned cans as the pipes they used, while 3/20 used inhalers as a common tool to smoke crack. In B20, it was noticed that most participants mentioned two similar tools to smoke crack, glass bottles (7/20) or plastic water bottles (5/20).

Comparatively, the reasons for choosing a particular pipe are focused mainly on the availability of the pipe. In N07, 4/7 reported that the reason behind their choice is based upon the availability of the pipe. While the efficiency, pleasantness of the pipe, and the cost choices were reported only once for each. Two participants mentioned either personal preference or the health impact of the pipe may be the reasons to choose a certain pipe. The main reason to choose a pipe in B20 was availability (8/20). In B20, more participants were interested in pipe efficiency (4/20). Only one participant mentioned that he chose depending on the pleasant hit he got from using a certain pipe. None of the 20 participants mentioned the cost of pipes as a factor that may affect their pipe choice. Some participants gave other reasons behind choosing certain pipes, 2/20 commented on negative effects of using equipment that may need an ash layer in order to smoke crack because they have chest pain. Due to that effect,

they preferred to use glass pipes. Also, one mentioned some characteristics of the optimal pipe: easy to carry, easy to be dismantled.

The reasons for choosing the pipes reflected the sharing habit and the difficulties that were reported by crack smokers. The difficulties of smoking crack included mainly effects on the health of smokers, e.g. cut lips, burnt lips for the users who smoke by cans, breathing problems, cross contamination. In N07, the common difficulty related to using pipes was breathing problems, e.g. wheezing, coughing. Also, 1/7 emphasized cutting lips and burning lips as a result of using certain tools to smoke crack. The alarming comment was from 1/7 in this group, he mentioned that being arrested by the Police due to pipe possession could be a difficulty of using a proper or safe pipe everywhere. This could explain the use of disposable tools to avoid arrest in the street. In comparison, in B20, it is noticed that 9/20 mentioned related health problems as difficulties using some pipes. Chest pain and breathing problems were the common difficulties reported by the smokers, and also others mentioned sore throat or bad teeth. There were also other types of difficulties which were related to collecting or preparing the pipe. One of the participants summarised the situation when he mentioned that whilst a can is not an efficient pipe to smoke crack, it is easy to get a can when he is outside.

10.1.1.6 Sharing pipes

It is common to smoke crack within groups; smoking crack is associated with high rates of sharing pipes. In N07, 5/7 reported sharing pipes either due to lack of pipes, or because sharing is a social issue in a crack smoking environment. At the same time, 1/7 who reported that he does not share pipes, explained that sharing a pipe is dangerous. Also, in B20, 19/20 reported that they share pipes. More than half of them mentioned that when they smoke with others, they have only one pipe there to smoke. Others mention other reasons for sharing: “it is easier than making my own”, “it is not worth using my own if we have only one stone each”. In comparison in N07, 1/7 mentioned that he used to share without thinking about the risk.

10.1.1.7 Cutting agents

The pipes and cocaine are not the only source of health problems, but the cutting agents may be also responsible for associated health problems. Although all in N07 reported that the cutting agents have harmful effects, 2/7 reported that the cutting agents were sometimes harmful, whereas, 5/7 mentioned that the cutting agents were always harmful. In B20, 1/20 said that cutting agents do not have harmful effects, while 8/20 reported that cutting agents sometimes have harmful effects, and 11/20 emphasized that cutting agents always have harmful effects.

Regarding participants' knowledge in both groups about the type of cutting agents used in the crack they smoke, in N07, 2/7 said that they did not know what cutting agents might be added to crack samples, the other 5/7 reported ammonia, bicarbonate, and citric acid as cutting agents. Also, in B20, 1/20 said that he did not know what cutting agents were added to crack samples, while most other participants reported bicarbonate and ammonia as cutting agents. In B20, different substances were included in the cutting agents listed by participants, e.g. novocaine, benzocaine, baking powder (sodium bicarbonate).

The motivation of users can lead them to check the quality of the samples they buy on the street. In N07, 4/7 participants check the quality of samples by different ways, e.g. looking, feeling, smelling, tasting the samples, and other ways. On the other hand, 1/7 reported that he did not check the quality. One of the participants did not answer this question; he may be not interested in checking the quality of crack samples. The reason for checking by these participants is looking for quality. In B20, 9/20 check while 10/20 do not check the quality of samples, 1/20 did not answer this question. Regarding the ways used to check the crack quality, 4/20 reported that they check their crack by looking only, while 0/20 check the crack by feeling, and 2/20 taste their crack to check the quality. Only 1/20 mentioned that his buying decision may be effected by checking the quality of the crack.

10.1.1.8 Source of information

The participants' knowledge about cutting agents' effects, pipes, sharing pipes, and other habits of using illicit drugs comes from different sources. In N07, 4/7 reported other users as one of their information sources, while non-user friends were

sources reported by 3/7. Family was a source of information for 3/7, and drugs services for 4/7. News and the internet were reported by only one participant for each. Doctors were a source for 4/7, while personal experience was chosen by 5/7 as the common source of information about crack in N07. On the other hand, in B20, it was noticed that the main source (8/20) of information about crack was other crack users. Non-user friends and family were reported by two participants for each as sources. Moreover, drugs services and personal experience were mentioned as sources (3/20), while books and doctors were only reported once for each as a source.

10.1.1.9 Drug Services

One of the reported sources for information was drug services. The participants were asked “how many times in the last two years have you engaged with drug services to support your crack use?”. In N07, 3/7 have engaged in the last two years. The engagement was varied between the three who reported that. This could be caused by the shortage of services provided for crack users compared with users of other drugs. The 3/7 reported that they engaged 2, 5, and 48 times. In B20, 8/20 have engaged with drug services to get support about crack use during the last two years and their frequency of engagement in B20 varied between 1-6 times. There are many reasons behind the limited times of engagement with drugs services. The first could be that there is no treatment or even no substitution treatment such as methadone for heroin addiction, even new studies show only a limited potential for novel compounds to treat crack dependence [141]. Also, in the case of smoking crack, in the UK it is illegal to supply any pipes and tools that can be used for smoking unlike supplying needles and other kits that are supplied for heroin addicts and other IDUs.

This can be explained when all the participants in N07 reported that they engaged with the drug service for heroin, where they receive substitution treatment and needles and kits for safer injecting. Also, 2/7 engaged with the benzodiazepine service and one engaged with the cannabis service. In B20, 17/20 engaged with the heroin service, which could be evidence about the effectiveness of supplying services for illicit drugs. Only one engaged with the amphetamine service, and 3/20 reported that they engaged with the benzodiazepine and ketamine services, respectively. Two out of twenty engaged with the cannabis service in B20, while 5/20 engaged with the alcohol service compared with none in N07.

The reason behind most participants engaging with the heroin service could be explained when they answered the question about the availability of glass pipes. In N07, 6/7 agreed that if safe glass pipes were available from a local drugs service, people would be encouraged to access the drugs service more. Those participants commented on this answer that available pipes could provide users with quality equipment, safer ways to smoke, and so reduce harms. Also, 1/7 said that it could be similar to a NEP. Only 1/7 did not agree with the statement of the question. In B20, all participants (20/20) agreed that if safe glass pipes were available from a local drugs service, people would be encouraged to access drugs services more. The comments of participants in B20 focused on certain points. If the service would supply free pipes for smokers this could attract them to engage in the service to receive information and other related services. Also, they mentioned that having pipes available could be a good HR tool, supplying clean tools for smoking crack and so reducing harms. This could also reduce the crime committed to get money to buy pipes.

10.1.1.10 Follow-up stage

The follow-up for this group was carried out after two weeks for N07 and after four weeks in B20, due to limited time to finish the study. The participants, after the first stage when the intervention was delivered to them, received the modified questionnaire to measure their smoking habits, knowledge, pipe choice, the impact of the intervention, and their expectations about the efficiency of similar interventions.

In N07, the norm of using crack cocaine indicates that smoking crack is mainly 2-6 times a week (3/7). Two out of seven of this group reported that they smoked once weekly, compared with others who either smoked once a day or once every two weeks. In B20, the norm of use is also mainly 2-6 times a week (10/20), 3/20 reported that they smoked more than once a day. Two participants mentioned that they smoked crack once weekly. While 3/20 reported that they had stopped smoking and injecting crack cocaine (Fig. 10.4).

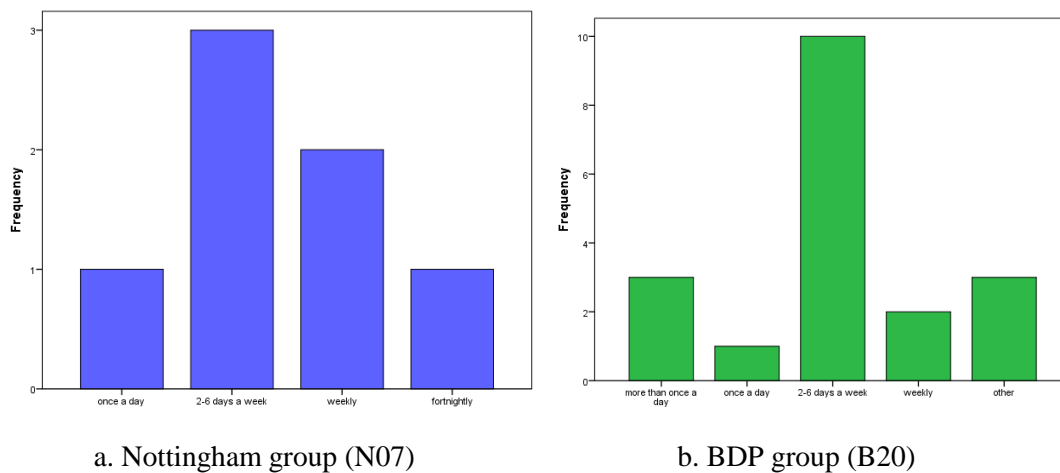


Fig. 10.4. Crack use norm in Nottingham and BDP groups (follow-up).

Although the stem pipe was used by 3/7 in N07, use of cans was also reported (3/7). There may be different reasons to use cans although they were informed about the massive waste of crack and harmful health consequences due to using cans compared with using other equipment. Looking into the reasons behind choice of pipe, users emphasize in two stages that the main reason is the availability of pipe equipment more than any other reason. The most commonly used pipes in N07 are still glass bottles and plastic water bottles. The reason for using specific pipes given in the baseline questionnaire was their availability. This can explain the use of some harmful handmade equipment compared with less harmful pipes. In B20, there were 3/20 who stopped smoking and injecting crack. Only 1/20 reported using a stem pipe, and 2/20 used inhalers to smoke crack. The majority of B20 (13/20) still use glass bottles and water bottles to smoke crack.

B20 participants were asked whether they shared any information about the intervention with others, 16/20 have done so. They reported that they shared various information related to health, efficiency of different pipes, and cutting agents. Some focused on the cutting agents and the effect on health, while others discussed the infectious viruses that may be transmitted via a shared pipe. Others were interested in the efficiency of various pipes, and the expected effective role of distributing clean pipes to smokers. Significantly, the shared information could show the acceptance of the intervention by participants, although one of them shared the given information and another talked with 5 people about it, one mentioned that the questions were silly. Two smokers shared the information about the infectious viruses that can be

transferred by sharing pipes, which most smokers thought is only related to sharing needles.

N07 participants were asked in follow-up, the reason behind their choice of the pipe they use. One of the messages in the intervention was to present the different emitted doses of cocaine from the different common crack smoking devices. Was efficiency one of the reasons for choosing the specific pipe? In the follow-up stage, 4/7 participants chose efficiency as a parameter when they used a pipe compared with only 1/7 in the first stage of the study.

Regarding difficulties mentioned due to using a specific pipe, besides the difficulties that were mentioned in the first stage, the crack smokers in N07 reported more difficulties related to using certain pipes. A smoker who used a medical inhaler as a pipe mentioned the melting plastic and inhaling the fumes of the molten pipe. This can lead to additional dangerous health consequences of using medical plastic equipment which was manufactured for asthma patients. Another smoker, who used a stem pipe due to efficiency reasons, stated that he was arrested due to carrying the pipe. The smoking of crack cocaine did not change between the baseline and the follow-up questionnaire two weeks later.

In B20, the participants were asked a question about the vouchers that they received in the first stage and how they spent them. Most of them reported that they either bought food, clothes, kitchen-ware or they gave it to others to support them, while only one mentioned that he sold the voucher.

Although the participants in general gave feedback that most of them know that cutting agents are either sometimes or always harmful, many of them mentioned bicarbonate and ammonia as the only cutting agents they know. This indicates their limited knowledge about the nature of the cutting agents used and their consequences for health. So, designing interventions that inform users about the hazardous health problems and harms associated with using certain handmade equipment and consuming cutting agents may be helpful in HR.

In both groups, the friend is the main person in common who shares the first experience of drug abuse. Therefore, friends should always be involved in implementing interventions and materials that can encourage users to avoid problems and habits associated with their risky behaviours.

10.1.2 Discussion of Quantitative part

The results reported from the questionnaire in both groups covered various points. The disadvantages of smoking or injecting crack brought many health problems. Skin problems are associated with injecting drugs as reported by Murphy and co-authors [142]. They found that injecting drugs by IDUs was one of the major risk factors for abscesses. Various types of injuries may include related pathogen-derived injuries, e.g. HIV, HCV. Also, using dirty needles and sharing those needles and other paraphernalia can transmit bacterial infections and viruses among users. One of the main risk factors of abscesses is injecting a mixture of cocaine and heroin “speedball”. Injecting two drugs may cause irritation and tissue damage due to the synergistic effects of the mixture and also the frequency of injuries could lead to an increase in vein damage. The further development of such injuries may be caused by a delay in seeking treatment. Therefore, it was recommended to optimise drug educational and alternative interventions to minimize those problems [142, 143].

Further problems associated with using crack include committing crimes and being involved in violent activities. This agrees with Lightowlers and Sumnall’s [144] research that showed the effect of drinking alcohol and using cocaine on predicted violent behaviours for the young people involved in their study. So, they recommend giving more attention to the violent behaviours associated with drug use and being involved in the intervention provided to reduce alcohol and drug abuse [144, 145].

The results also show the role of friends when starting to use drugs or even starting new behaviours. Friends could therefore be engaged to change some behaviours that may lead to hazardous consequences. Others start with either a group or a boyfriend. This agrees with the results of Cohen and Sas in their study about cocaine users in Amsterdam in 1993, where they found at the baseline that a friend was the main companion who started cocaine use with him [113]. Also, this agrees with what Nation and Heflinger published about the role of peer relationships as one of highest psychosocial risk factors in adolescent alcohol and drug abuse [146]. Additionally, HR interventions could be delivered by a drug worker who has a good relationship with the drug users to be able to deliver any such service or intervention. The acceptance of others experience or receiving information could be strongly based on such a relationship.

The results revealed the accessibility of crack samples in the street. They may clarify the market of crack cocaine and that it is available everywhere and so no need to prepare it or be at risk by having tools or materials used in cooking crack. The pipes availabilities and utilization were varied and based on several parameters. One of the participants said that he uses cans outdoors, while he uses a plastic water bottle indoors. Although the participants had a knowledge and awareness about the problems of sharing, it was a common risky behaviour between most crack smokers. Therefore, reducing sharing pipes and other smoking equipment should be a main aim of interventions to reduce those harmful consequences of sharing. Sharing drugs is also a common behaviour besides sharing pipes.

Compared to the availability and provision of substitution therapy and various HR paraphernalia for the use of other drugs, none is available for crack, this makes smoking crack associated with more harmful problems. This should encourage HR interventions to reduce those problems and push towards amendments of current policies with respect to crack use. This also agrees with the cocaine users who participated in the Cohen and Sas study in Amsterdam when they preferred to have a cocaine policy, like that existing for heroin, which is less restrictive than the current cocaine policy [113].

The limitations of both groups are that they include only a limited number of participants. More participants are therefore required in order to be able to generalise the findings and the recommendations. Also, all participants in N07 came from the same background, all are white British, and also the majority of participants in B20 have the same ethnicity which may not represent the diversity of people in the community. This can make the results biased as some behaviours may be correlated with cultural issues. However, six of the participants are male, while only one is female, and 15/20 are males in B20. This can lead us to miss some details that might be related to female behaviour especially for sex-workers who may use crack in specific situations.

The responses of participants did show sharing the information of the intervention with other crack users. So this information for smokers is important and they may not have such information about this kind of substance before. This could be interpreted from the baseline data where the smokers mentioned examples of cutting agents. There most of them mention only bicarbonate and ammonia as “cutting agents”, the bases used to free cocaine from its salt.

There is a current argument about participants using vouchers to buy drugs. Vouchers can attract more people to be involved in similar studies to get more information about the projects. Also, more people can share their experience and knowledge about the study questions which can help in the design of interventions. The results of this study using modest economic compensation for participants agree with a previous study [147] that showed that providing the participants with incentives could be an economic gain for them, but also it could be a useful source of information about drug users experience. It is a way to encourage users to talk with drug workers without judgement, and possibly to provide them with information and drug services. A main outcome of this study was that crack smokers participated for key reasons consistent with altruism and drug-use motivation [147].

One of the recommended changes for crack users and smokers is to supply a pipe to smokers through drugs services similar to the provision in NEP. Six out of seven participants in N07 emphasized that if safer pipes are available in drugs services, this will encourage smokers to access the services. The participants reported different reasons for the supply of safer pipes to smokers and the access to drugs services, for example they focused on the quality of the equipment and the harms that could be reduced. Also, one of them mentioned that supplying pipes to smokers can be similar to NEP to provide users with safer kits which can reduce transmitted viruses [108], and avoid cut and burnt lips and fingers caused by using handmade equipment e.g. cans, glass bottles, and water bottles.

In the UK, there are similar programs that are based on the same concept of supplying safer materials for illicit drug users to reduce or prevent dangerous consequences. Pizzey and Hunt [148] concluded that supplying foil for heroin users as an intervention can encourage the users into reverse change, to chasing heroin instead of injecting it. The feedback from their users emphasized the role of foil for chasing heroin as an aim of the intervention. The outcome showed that the self-reported behaviour change by supplying the foil and discussing with the users about the benefits of using foil instead of injecting heroin. Also, this helped the users to be more engaged in the services provided via health and social workers. The legal consideration of supplying equipment and tools to administer the controlled drugs follows Section 9a of the Misuse of Drugs Act (1971). The amendment of this Section exempts the supply of needles, syringe, water, filters and citric acids, but foil is not yet on the list to allow workers to provide foils to users [148].

Another report about the role of supplying foil to users came from the National Needle Exchange Forum (NNEF). The NNEF consists of about 600 members in the UK; it involves needle exchange managers, workers, supporters, and drug users. The report concludes the results of a survey by NNEF about the supply of foil via NSP. The foil is considered as a HR tool to encourage heroin users to change from injection to a safer route such as chasing in the case of heroin. Most participants emphasized that supplying aluminium foil could help to bring about an important decline in the behaviour of injecting and encourage users to chase heroin instead. Also, the response of NSP workers was that they did not supply foil due to legal issues. The majority of participants had the same idea that the law should be changed, foil should be supplied in NEPs [148, 149].

The educational interventions should be mixed interventions using more than one element. The evidence base of educational intervention only is not good enough to achieve a change in drug users' behaviours. The educational element is a main element that can lead to a behaviour change, but it should be used with other elements such as motivation or skills to develop a model that can be applied to test the mixed intervention as HR to change drug users behaviours.

10.2 Results and Discussion of Qualitative data analysis

The process of analysis started with coding step one. Coding commenced with primary coding which summarized and continuously extracted every piece of data. The themes were drawn mainly against the IMB model constituents and any other main theme that could be found, as identified by the HR workers who participated in the focus group and interview sessions. The questions of the focus group and the interview were prepared based on the delivered intervention material and the participants' experience of communicating with drug users to explore the efficiency of the PIPES tool. The questions were divided into the following categories:

1. The impact of presenting the results of emitted dose from different pipes and the hazards associated with using those pipes.
2. The effect of presenting analytical results of street crack samples and the effects of the main cutting agents on health.
3. The effect of discussing with and informing crack smokers of HR tips that they should practice to reduce some dangerous consequences.

4. Discussing the possible impact of supplying safer tools to smoke crack and the consequences of this strategy.
5. Discussing the limitations that were faced during the study and how the intervention could be optimised to promote positive outcomes.
6. General views about services available to crack users.

10.2.1 Results of Qualitative study

The IMB model determines that information, motivation, and behavioural skills have direct impact on behaviour; information and motivation also have indirect impact on behaviour through their effect on behavioural skills. For that, any intervention designed based on the IMB model will effect behaviour through its effect on IMB components [32]. The results of the questionnaires could be confirmed and explained through probing the data collected from HR workers. The behaviour components could support a view that could be used to design similar interventions or further tools in the case of crack use. Data are presented below under the overarching themes of the IMB model.

10.2.1.1 Knowledge

One of the most common comments of HR workers about the presented information in the intervention was that the crack smokers did not know before about this topic and did not know any difference between using various pipes. The workers also said that the smokers did not have enough knowledge about the health consequences of using crack or crack pipes (in the following, *Q* signifies a direct quotation).

QN07 'A few of them obviously didn't realise which one was causing them the most damage and not getting a higher dose'

Although the emitted dose for each pipe was of interest to some smokers, it was reported that they started thinking again when they were informed about the consequences of using each pipe. This could indicate the importance of informing users about health issues related to their drug use behaviour, and suggests that they do not know “everything” about the drug and the route of administration they use.

QB20 (F) 'They were really interested in the dosage at first or the different kind of pipe, but then when you highlight the risk of the red, amber, green it can make them stop and think a bit more'

Although the crack smokers knowledge was seen as very important when choosing the less risky equipment to smoke crack, their choice is also dependent on other parameters and circumstances. Availability of pipes is a determinant for smokers even if they do not prefer to use some risky tools. The workers mentioned that smokers usually choose the pipe depending on the place where they smoke. For example, a smoker could use a can when he wants to smoke in a street, and this is commonly done by irregular users. Other regular users who prefer to use other tools, e.g. glass bottles or plastic water bottles, smoke at houses or safe places. The choice of regular smokers was not thought to be based on knowledge of pipe differences or associated risks, but on the convenience of the equipment. Regular and irregular smokers were thought to have a lack of knowledge related to the emitted dose of different pipes and the health consequences for each one. This could be a further reason to provide crack smokers and other drug users with more information about the drugs they misuse and the risks from the route of administration.

QN07 'Overwhelmingly availability and ease of access, easy to get hold of'
QB20 (F) 'A lot of them were unaware of the risk of the inhaler so it did highlight that for them they were quite shocked at that... some of them... which was interesting'

The workers confirmed the usefulness of the information in the intervention. They said that they felt that this information is interesting for smokers and could have a positive effect on their pipe choice. The Nottingham HR worker said that 2/7 changed the pipes they use, they started using glass bottles to get rid of the problems associated with their previous equipment. This is an example of a desirable outcome of providing information to crack smokers to encourage them to use less risky tools.

QN07 – 'I say a couple of them had actually changed their choice of pipe to a glass bottle'

Lack of knowledge was thought not only to be related to cocaine, pipes, and emitted dose of different pipes, but also to the cutting agents and the health consequences that are caused by such cutting agents. The workers confirmed the questionnaires' results which revealed that crack smokers do have a lack of

knowledge about the cutting agents. They did not know any name for any cutting agents. Although they know that crack samples are impure and most of them mentioned that cutting agents have sometimes or always harmful effects. This may indicate lack of awareness about health consequences caused by cutting agents.

The HR worker in Nottingham said that the smokers did not have awareness about the effects of contaminants and they did not name any of the used cutting agents. He said that participants reported that samples are cut with white powder or mixed with tablets which indicates a low level of knowledge about this problem.

QN07 – They've seemed to be an awful lot of lack of awareness of contaminants that [it's] cut with...that's what I'm saying, they did not name any contaminant not even the stuff that's used

Also, the BDP HR worker mentioned the same idea that crack smokers are unaware of cutting agents or their consequences and even they had not heard about phenacetin which is now one of the most common cutting agents in crack cocaine samples. The users were interested to know more about phenacetin as a cutting agent and its sources. This could increase their knowledge and awareness about what is actually in the samples they smoke.

QB20 (F) 'They were all pretty unaware of the phenacetin and they used all other kind, bicarbonate, ammonia lots of other materials they were mentioning'

10.2.1.2 Motivation

10.2.1.2.1 Motivation about smoking model pipes - health problems

Three HR workers said that informing users about the emitted dose and the dose and risk difference between pipes was of interest to the smokers, motivated them to be more involved, and to discuss their behaviours. They felt that this may help some crack smokers to think about their pipes, change what they use, finding other available tools depending on their understanding of the information in the intervention.

QN07 '...didn't realise which one was causing them the most damage and not getting a higher dosechanged their choice of pipe to a glass bottle'

QB20 (F) 'They were really interested in the dosage at first or the different kind of pipe, but then when you highlight the risk of the red, amber, green it made them stop and think a bit more'

10.2.1.2.2 Motivation about phenacetin and cutting agents

The crack smokers were interested to know more about the cutting agents and phenacetin in particular. Although most of them knew that cutting agents have sometimes or always harmful effects, none of them named phenacetin or other cutting agents. This could reflect a lack of knowledge in this area. They wanted to know the sources of phenacetin. This may reveal the curiosity of crack smokers to know more about the samples they use and why those substances are added and from where.

QN07 'That people are aware... because obviously you're not going to know 100% what you put into your body'

QB20 (F) 'They were really interested in where it came from and how people were getting hold of the phenacetin'.

10.2.1.2.3 Motivation about availability

Crack smokers asked workers about glass pipes and how they can get them. This may reflect an impact of the intervention and the information about the different pipes given, and how the glass pipe could be safer than other equipment. This is of interest as it does not give the maximum emitted dose of cocaine compared with others, dose which may be expected to be the priority. Crack smokers' interest about getting safer pipes could suggest their attitude towards their health gives it more importance than simply getting more cocaine.

QN07 'They were happy to take that if pipe was safer'

QB20 (F) 'They were really happy to take part [in the study], but they didn't think they'd get a lot from it themselves there and then, but they knew in the future it might help [others] - but they were quite happy to have the shooter on offer as soon as possible'

10.2.1.2.4 Motivation to share knowledge

The crack smokers were interested in the knowledge they got through the intervention and they mentioned, in the follow-up questionnaire, that they shared the

information either in part or in full with other users. Although the intervention could not (legally) supply any alternative equipment for crack smokers, it encouraged them to talk with other smokers about the differences between pipes, the risks associated with different pipes, and about the cutting agents and their harmful effects. This may show that smokers want to share knowledge and information to help their peers. The HR worker in Nottingham was also interested to present the intervention to the Commissioners of Drugs Services, to encourage them to include it in the services that are delivered in his area to crack smokers.

QN07 'Every single person commented this is really impressive, really informative, good information'

QN07 'I'd like to present that information and the little report to our Commissioners'

QB20 (F) 'They were sharing about the phenacetin with them so obviously it triggered some interest in some of them'

10.2.1.2.5 Future investment

This research was the first attempt to use the results of pharmaceutical analysis to inform crack users about risks, without any possibility to supply alternative pipes, due to legal issues. Crack smokers were interested to push this research forward and they hope to get more progress in the future which may provide future smokers with safer equipment to reduce associated harms. This may show the altruism of smokers towards other smokers and their belief of the importance of changing the regulation to get safer equipment to smoke, to get the same deal as IDUs who can get clean needles and paraphernalia for free, e.g. NEP.

QB20 (M) 'Interesting investing in the future of crack smokers, it almost contests that kind of potential not selfishness, but that kind of individual world that people might exist in using sometimes, but having an impact on future service users'

10.2.1.3 Behavioural skills

10.2.1.3.1 Sharing pipes

One of most common behavioural habits between crack smokers is sharing equipment to smoke crack. Although crack smokers mentioned that they share their

own equipment with other smokers due to various reasons, e.g. they do not have pipes, they wanted to share crack rocks. The HR workers added that some smokers share their pipes to recycle the residue at the end of day and get a “free smoke”. For that, they prefer to get equipment that is easy to recycle and wash to get the residue and smoke it. Disposable pipes may therefore not be used as intended (i.e. single use). This could be useful information to inform whether safer pipes could be designed in future to produce equipment to make smokers more interested to use them and therefore to avoid using dangerous equipment.

QN07 ‘The sort of stuff I expect them to know and they didn’t cause we’ve done training around BBV and not sharing their stuff either which a lot of them got, but sometimes they had to be drawn out’

QB20 (M) ‘Culture of people wanting others to share their pipe’

QB20 (M) ‘You’re passing a pipe round and you could accumulate that sort of stuff quickly. The feedbacks on the client that for the truck to wash this pipe ‘woo hoo’ the day has finally come where I can do this from letting everybody use my pipe’

10.2.1.3.2 Choosing pipes - health problems and how this could be changed

Choosing pipes or equipment to smoke crack is related to many parameters depending on the place where they smoke and the frequency of smoking. The HR workers mentioned some cases and conditions for smoking. For example, the smokers who used to buy a crack sample in the street and smoke it there, they usually use cans due to availability and ease of use, then throw them away. Moreover, irregular users usually use cans or other available tools, while regular smokers prefer to have a convenient pipe or equipment to use when they smoke. This could show the role of place and smoking tools based on history and regularity of crack use.

QN07 – ‘Changed their choice of pipe to a glass bottle’

QN07 – ‘Couple have actually reduced crack use’

QB20 (F) ‘If it’s someone who is not smoking every single day, that is for example may bump into somebody and they’re out on the street, then they’d go for a tin can because it’s quick and easy’

QB20 (F) ‘Some of them would chose the inhaler, a lot of them were unaware of the risk of the inhaler so it did highlight that for them, they were quite shocked at that, some of them, which was interesting’

10.2.2 Discussion of Qualitative study

Smoking crack cocaine by using handmade or makeshift equipment is linked to increased risks of getting burns, cuts, and other injuries for the hands, lips, and face. The consequences of those risks are associated with the possibilities of acquiring an infectious disease, e.g. HCV, tuberculosis, and pneumococcal diseases through sharing equipment. Moreover, using some material to smoke crack incorrectly, like a metal mesh, is also associated with inhaling hot pieces of steel and glass fragments [150-154]. It is concluded that the crack smokers' lack of knowledge contributes to their taking such risks. This was investigated by the questionnaire which was conducted with crack users and the interviews of workers in HR drugs services. It was noticed that most participants rely on their personal experience to get information about crack and other drugs, and they did not name any cutting agents that have been previously determined in drug samples. Most of these cutting agents are known to be harmful pharmacologically and some have been withdrawn from human treatment, e.g. phenacetin, levamisole. The knowledge of the participants was limited about the differences between common equipment for smoking crack and the risks associated with each one. Sharing the smoking tools may have similar infection risks, but the material equipment may cause specific health problems, e.g. using plastic equipment which gives off carcinogenic fumes when hot, or sharp glass or tin cans that are associated with inhaling ash or glass shards that may cut lips or fingers. This may show the importance of designing an intervention to increase the knowledge of crack smokers using laboratory results from analysing seized crack samples. The findings showed that most participants were interested in the information in the intervention and they were motivated to share the information with other users after the first session. Many mentioned in the follow-up that they talked to other users about what they learned. Also, the participants showed a high level of altruistic motivation towards future drug users and they were interested to provide them with available safer pipes to reduce the risks associated with the makeshift equipment they use currently. This agrees with the motivation behaviour of drug injectors towards providing methadone for drug users who suffers from withdrawal symptoms of opiate addiction [155].

The main limitation for this study is supplying participants with information only about the tools they use to smoke crack while it is still illegal to supply them

with safer pipes or equipment that could be used to reduce some of the associated problems with the makeshift tools they use currently. HR workers commented on some limitation to encourage crack smokers to start taking action towards using safer equipment. Although workers valued the importance of increasing the knowledge and awareness of crack smokers to reduce health problems, they emphasized that to gain the desirable actions, it is essential to provide safer pipes or equipment with the intervention delivery.

QN 07 'They require glass pipes'

QB20 (M) 'When we can give them the equipment to be able to take action around that, then they will do it, so if we were able to go 'here's a glass pipe' ...

Leonard and co-authors reported [85] a modest decrease in sharing smoking associated with supplying smoking kits to crack users. The most fascinating outcome was the significant decline in injecting drugs and an increase in smoking crack. The transition from injecting drugs into smoking drugs was one of the public health objectives due to the high risks associated with injecting as a route of drug administration [85], while Malchy and co-authors, and Boyd and co-authors [156, 157] reported sharing pipes still occurred although safer pipes were supplied. Their explanation of this sharing behaviour is based on different reasons, e.g. sharing pipes is a social networks habit; inadequately supplying kits where the kits were supplied one per user. This made the availability of safer kits limited and not a continuous process. It was noticed that there was still the use of harmful pieces of metal instead of the supplied safer mesh-screens due to a lack of awareness of the hazardous health consequences of using Brillo (metal mesh pieces). They recommended the necessity to find effective HR messages to be associated with supplying safer kits over the concerns of such harmful behaviours. They also recommended accompanying the supply of kits with effective HR messages about the harmful effects of sharing equipment. They found that educational HR messages were successfully transferred by demonstrating safer practices, watching others practising, and informal discussions with users [156, 157]. The impact of providing safer alternatives was measured in the questionnaire through two main points. The first was when crack users gave "lack of equipment" as a reason to share pipes because many of them mentioned that they used to smoke in a group where they have only one pipe. The second point was when the participants were asked whether they will collect the pipe if supplied by drugs

services. All of them answered yes and they preferred to have a program like the well-established NEP.

Comparing with the UK experience towards HIV, NEPs were successful to respond to the epidemic because information to avoid sharing paraphernalia was combined with sterile injecting needles, while it was reported to be less successful in other counties where only information was provided to drug injectors. Moreover, it was noticed that supplying IDUs with citric acid sachets within NEPs helped to attract IDUs to the service. This opportunity may increase the possibility to provide safer injecting services and interventions. According to the Misuse of Drugs Act (Section 9A) (at least until August 2003), it was illegal to provide any paraphernalia to IDUs. The only exemptions at that time were needles and syringes to prevent HIV transmission. The Act was amended in 2003 and in 2005 to allow the legal supply of some paraphernalia, e.g. citric acid, ascorbic acid, spoons, swabs, filters, and sterile water [158].

Crack samples are usually cut with various substances, some of the cutting agents are harmful and cause dangerous consequences [25]. Although the participants in the questionnaire answered that they believe that cutting agents have either sometimes or always harmful effects, they did not name any of the cutting agents which were usually identified in crack samples. In this study, it was surprising that most participants had not heard about phenacetin, which is considered to be one of most common cutting agents for crack samples and they did not know anything about its effects [22, 25, 159]. They were interested to know more about this cutting agent and its sources. This shows a lack of knowledge about cutting agents and their health effects, but a willingness to learn. All of this raises the need for further educational messages and training for drug users about such cutting agents.

In the case of crack smokers, there is no treatment for crack cocaine and there is no available service unlike the substitution therapy or safer kits in drug service programs aimed at opiate users [160]. This makes crack smokers marginalised and there is therefore a lack of reason for them to visit drugs service centres. This HR intervention was a route of engagement for crack smokers which was welcomed by the HR workers. They emphasized that the intervention was a successful way to encourage crack users to come to the drug service centre and to talk to drug workers. This could be a way of promoting engagement with other available services, because they have an opportunity to deliver information and services to less usually seen

clients. More progress in engagement could be achieved by personalising the designed intervention according to the HR workers' recommendations through measuring the efficiency of more smoking tools and then delivering the tool that really relates to the participants to make them feel important and cared for.

This HR intervention was mainly aimed at increasing the knowledge of participants towards the efficiency of different smoking tools, cutting agents and their effects, and HR tips for smoking crack. There was only a short time and only one session. The study was somewhat limited by time to conduct any further sessions and the time required to conduct a longer follow-up questionnaire. The designed intervention and the results of the two questionnaires showed the lack of knowledge and communication with this category of drug users. More research is therefore needed into informing them about the dangerous equipment that they use, and designing more interventions to encourage them to engage with available drug services in order to reduce their harmful smoking habits.

The intervention was conducted for one session and the follow-up stage was 2-4 weeks from the baseline questionnaire. This does not provide evidence of any sustainable long-term change in knowledge or behavioural skills of crack smokers. Future work will have a further follow-up after a longer time to measure any change or impact on behaviour elements. Using similar samples, more cutting agents could be presented. HR workers said that users did not know anything about this. Another suggestion made by workers, to engage more smokers in this type of intervention, was to use more diverse crack samples and a greater range of smoking tools. This can help to design personalised interventions which may make the participants feel that this was designed for their case and make them feel involved more in the intervention.

QB20 (M) 'If you had the data for 10 different smoking devices you get someone say which one do you use and then you have that data for that specific one you might increase the engagement with someone because they might believe it was more specific to them'

In this study, the crack samples were provided by the Swindon Police, and then the intervention was delivered to crack smokers in Bristol and Nottingham, so the participants may not care about the content because crack samples may have different contents in different places. Also, the samples were seized a few years ago, while current samples have a different (lower) purity as reported in national reports and

published papers reflecting the downward change in the purity of cocaine and other illicit drugs in recent years [17].

QB20 (M) 'the locality and recentness of the samples might make it more individual and I suppose make them feel more likely the intervention was something that was being designed for them'

Bringing together the above recommendations for possible future work, interventions could be optimised through some of the suggestions of HR workers mentioned in the focus group. They commented on the date of seizing the crack samples that were used in the analysis to design the intervention. These are old samples and the content of current crack samples may have less cocaine and/or different cutting agents in Bristol and Nottingham where the study was conducted. The HR workers also suggested designing personalized interventions. This may encourage the participants to engage in the research and interact positively with the content of the interventions. Due to continuous changes in the content of crack samples and the tools used to smoke, continuous training and updating of the intervention content is required to keep the participants up to date and engaged in the drugs services.

Chapter 11

Conclusions

11.1 Conclusions from the pharmaceutical analysis of crack samples

The annual reports of UNODC and other published papers show the changes in purity of crack cocaine during the last few years and in the cutting agents used. Crack purity has decreased markedly which may increase the effects of cutting agents especially those that have serious side-effects. This, together with using hand-made equipment as tools to smoke crack, could be responsible for the current high risk health problems.

The purposes of the laboratory phase of this study were to determine the analytical profiles of seized crack samples. Profiling techniques included qualitative and quantitative pharmaceutical analysis aimed at identifying cocaine purity and cutting agents, and the study of the thermal behaviour of crack cocaine samples under different conditions. This study aimed to apply statistical analysis to the NMR data to identify potential commonalities in samples sources and distribution networks in seized crack samples. Crack cocaine is smoked using various types of handmade equipment. One of the aims was therefore to design and optimise a smoking model to evaluate the efficiencies of those devices under simulated smoking conditions. An applied research project was then undertaken to design and evaluate a HR intervention based on the results of the pharmaceutical profiling and other analytical procedures. The intervention to be delivered by HR workers to crack cocaine smokers. It will then be evaluated to determine the impact of pharmaceutical analysis results with respect to crack cocaine content, the cutting agents, and the different efficiencies of used devices on smokers' knowledge and awareness of the associated health problems of using makeshift pipes.

In the analytical profiling, HPTLC, FTIR, NMR, and EI-MS were used to identify cocaine, the cutting agents, and possible minor impurities. HPLC and GC were used to quantify the cocaine content and the main cutting agents, i.e. phenacetin, benzocaine. HPTLC, a simple, rapid and low cost method, produces a bar-code like profile of components and impurities. Compounds were identified by the use of authentic standards and specific reagents. HPTLC is potentially straightforward for

the lay drug-user for comparing the identity and purity of seized samples. It shows the similarity and differences between various batches of crack samples.

FTIR gives further information about the content, although the complexity of the spectra means that they are unlikely to be understandable to the lay drug-user. FTIR could be used in statistical analyses which may enable tracking the sources of drug and impurities. EI-MS provided information about compounds' molecular weights with expected formula and provided an understandable bar-code of purity. Also, it was used to identify the by-products of thermal degradation of cocaine in smoking experiments. Proton NMR spectroscopy provided both qualitative and semi-quantitative results. Various NMR experiments, including 1D and 2D spectroscopy, were used to confirm the structures and identify the components in the mixtures.

The quantitative techniques were GC and HPLC. The use of GC is limited to analyse volatile or derivatized compounds in order to avoid the possibility of blockage of the chromatography column. In this case, the aqueous layer could not be injected without pre-derivatization which would make the profiling method more complex and more time consuming. As well, quantification using this technique requires an internal standard. The reference sample was analysed by GC-FID and this method showed that this sample contains 42 % cocaine free-base and 33 % phenacetin. The routine practical technique to quantify samples' contents is HPLC. It can be connected to different detectors which give it high sensitivity and the ability to detect and quantify a wide range of compounds. A profiling procedure could be carried out depending on the samples and the desired outcomes of the study. Also, availability of equipment and skills of interpretation of results can sometimes limit using some techniques. HPLC was used to quantify the content of seized crack samples and to quantify the amount of cocaine and phenacetin in the model crack smoking experiments. The seized samples contained 24 % cocaine base and 32 % phenacetin. Those samples also contained some samples provided as crack samples, but they were found to be negative for both cocaine and any cutting agents (e.g. they were a powder of dust). Due to this, only drug samples were included in the statistics and they contained 33.7 % cocaine and 45.8 % phenacetin. Although the samples were seized in one area, their content was varied which could indicate the diversity of sources and adulteration processes at different levels. Analysis showed a similarity in the content of some samples that may originate from the same source. This could provide more evidence to track the samples' origins and drug distribution channels. The results of

analysing the reference crack sample that was used in crack smoking experiments showed that it contained 45 % cocaine free-base and 34 % phenacetin.

Proton NMR data were then subjected to PCA and HCA analyses in order to find any possible link between samples and thus potentially to track their origins and channels of distribution. PCA applied to the NMR data of the organic (CDCl_3) layer contents for 34 samples showed that the samples nearly all came together in one major cluster. Furthermore, the whole contents in DMSO, so not only the organic layer, of 112 samples were analysed using NMR and then PCA of those data showed the samples were clustered in one big cluster which represents the mixture of cocaine and phenacetin, with other smaller clusters for pure cocaine and for benzocaine. This can provide evidence for either police intelligence or forensic investigations about expected similarities between samples seized at the same or at different places. Also, providing evidence for studies of the drug market, changes of drug purity, and the cutting agents used. Whilst the present study showed this approach to be feasible, one limitation was the similarity of source of the samples analysed. A wide geographical spread of seized samples would provide a more robust trial of this approach.

The thermal behaviour of different crack samples may vary depending on many factors, e.g. concentration of each component, preparation procedures of illicit drug samples. The DSC profiles of the seized crack samples showed noticeable differences between pure and impure cocaine samples. In addition, DSC profiles showed differences between crack samples and mixtures prepared at the same concentrations, revealing the impact of preparation methods on thermal behaviour. Thus, even if crack samples have the same proportions of the same components, they may exhibit different thermal behaviour depending upon the methods used to prepare them. So this DSC technique could be sensitive to some characteristics that cannot be identified by other techniques. The DSC study showed the impact of high temperatures that lead to the degradation of cocaine. These results were used to optimise the conditions in developing a smoking model to measure the efficiency of common crack pipes which was used to determine the inhaled dose of cocaine and cutting agents.

Although there are various routes to administer cocaine, the common route to misuse crack cocaine is to smoke it by means of a crack pipe. The inhaled dose of cocaine and cutting agents could depend on the tool used to smoke, the conditions of smoking, and the concentrations of cocaine and the cutting agents in the sample. Using an optimised model under controlled conditions, less than half of the cocaine

and phenacetin in a crack sample was recovered from the smoking apparatus, while 15 % of the cocaine free-base and 16 % of the phenacetin were recovered from the smoking device (pipe). The inhaled amounts of cocaine and phenacetin varied between different smoking tools. The glass stem (Canadian shooter) delivered 39 % cocaine and 45 % phenacetin of the crack sample, while the drinks can delivered 31 % cocaine and 34 % phenacetin, and the medical inhaler delivered 47 % cocaine and 54 % phenacetin. This shows the different efficiencies across smoking equipment. Taken together, these results will be used in HR intervention design to inform crack smokers in attempts to reduce the problems associated with using some hand-made pipes. Highly toxic compounds (anhydroecgonine methyl ester, ecgonine) were identified as by-products of heating cocaine base under smoking conditions.

Smoking crack is safer than taking cocaine by injection. More experiments should be carried out to optimise smoking conditions that could reduce the highly toxic degradation products and reduce inhalation of cutting agents. Then the associated health problems resulting from those products of pyrolysis or from the effects of cutting agents on lung tissues would decline. The use of this optimised model with more crack cocaine samples containing various cutting agents would give a wider picture of the impact of different cutting agents on the inhaled dose of cocaine and the associated impurities.

The outcome was then used to design a HR intervention. This focused on many points, but the main one was to use the results of this pharmaceutical analysis study which showed the differences of inhaled doses of cocaine across various common pipes when the same crack samples were examined under the same conditions. These are major findings probably never quantified previously and never used in HR to-date.

11.2 Conclusions of the intervention study

11.2.1 Conclusions from the quantitative data analysis

These studies were the first to investigate, using a mixed methods approach, the qualitative and quantitative data arising from 7 (white British) crack cocaine smokers based in the Nottingham area (N07) with smoking and/or injecting crack experience over 16 ± 4 years. Their data and views are contrasted with the views of a second group of 20 drug users in the Bristol Drug Project (BDP) (B20) with average length of crack use of 17 ± 7 years. Fourteen of B20 are males, fifteen are white British, while

there are also three white, one Jamaican, and one Indian. Significantly, especially among attempts to gather such data from crack users, all the participants who started the study completed to the end in both groups. These users mainly and regularly (with a frequency towards daily) smoked crack, some also administered cocaine by both injection and smoking.

All the crack users agreed about the disadvantages of injecting crack cocaine. All of them mentioned the health effects, e.g. messing-up veins, BBV, abscesses. This indicates the level of awareness of crack users towards the negative impact of injecting illicit drugs. This can also explain the smoking habit for some drugs, and stopping injecting and turning to smoking the drugs instead.

The quantitative data show that nearly half of the participants (3/N07 and 8/B20) said that their first use of crack was with a friend. A wide variety of types and sources of pipes were used; the use of a medical inhaler was mentioned 3 times. The reasons for choosing a particular pipe are focused mainly, but perhaps not surprisingly on the availability of the pipe over efficiency, pleasantness, and cost. Health impact was rarely a reason, whereas ease of carrying and dismantling also featured. However, health problems were reported as difficulties in using some pipes. Chest pain and breathing problems were the common difficulties reported by some smokers, and others also mentioned sore throat or bad teeth. One participant summarised the situation in saying that whilst a can is not an efficient pipe to smoke crack, it is easy to get a can when he is outside. It is common to smoke crack within groups and sharing (19/B20) is a common social issue in a crack smoking environment, but there was recognition that sharing a pipe is dangerous to health.

In addition to the cocaine effects and to sharing the pipes, the cutting agents may also be responsible for associated health problems. All 7/N07 and 19/B20 reported that cutting agents have harmful effects, but they did not know what cutting agents might be added to crack samples. Most participants reported baking powder (sodium bicarbonate) and ammonia as cutting agents. Users rarely check the quality of samples, e.g. by look or taste, but this did not affect their decision to buy crack.

All 20 in B20 agreed that if safe glass pipes were available from a local drugs service, people would be encouraged to access the drugs service more. Significantly, 16/B20 shared the information they received in this intervention with others. In both groups, the results show that the friend is the main person who shares the first experience of an illicit drug. Thus, we should always recommend to involve friends

in delivering HR interventions and materials that can encourage users to avoid problems and habits associated with their risky behaviours.

One of the recommended changes for crack users and smokers is to supply a pipe to smokers through drug services similar to NEPs. Six of N07 emphasized that if safer pipes are available in drug services, this will encourage smokers to access drug services.

11.2.2 Conclusions from the qualitative data analysis

The themes were drawn mainly against the Information, Motivation, and Behavioural skills (IMB) model. Crack cocaine users are a difficult cohort to study. Unlike addicts with respect to smoking cessation, alcoholics, and opiate IDUs, crack smokers have little or no incentive to participate. This is the first study using questions of focus groups, structured interviews based on delivered intervention material, and the participants' experience of communicating with such drug users to explore the efficiency of the PIPES tool we have designed and prepared. In the case of crack smokers, there is no treatment for crack cocaine addiction, nothing similar to antabuse aversion therapy for alcoholics, and there is no available service like substitution therapy or safer kits in the drug service programs aimed at opiate users. This makes crack smokers marginalised, lacking real reasons to visit drug service centres. The HR workers recognized that this intervention was a successful way to encourage crack users to come to a drug service centre and talk to the drug workers and thereby receive information. All of this raises the need for further educational messages for drug users and especially about cutting agents.

One of the most common comments of HR workers about the information presented in the intervention was that the crack smokers did not know before about the topics that were presented. Nor did they know any differences between using the various kinds of pipes and the associated hazards and health consequences. Crack smokers usually choose their pipe depending on the place where they smoke, this is not thought to be based on any knowledge of the pipe efficiency or associated risks, but on the convenience of the equipment. Therefore it should be beneficial to inform crack smokers and other drug users more about the drugs they misuse, and the risks from the route of administration. The HR workers confirmed the usefulness of the information presented in the intervention, even leading some users to change their

choice of pipes, cutting down their health risks. This is obviously a desirable outcome of providing information to crack smokers encouraging them to use less risky tools.

There was a general lack of knowledge of cutting agents and the associated health consequences. Furthermore, informing smokers with information about the emitted dose, risk differences between pipes, as well as about cutting agents, was of interest to the smokers and motivated them to be more involved and to discuss their behaviours. Providing HR tips can reduce some dangerous behaviours. So, crack smokers asked HR workers about glass pipes and how they can get them. This may reflect an impact of the intervention and the information about the different pipes given, and how the glass pipe could be safer than other equipment. This is of interest as such a pipe does not provide the maximum emitted dose of cocaine compared with other pipes. This might have been expected to be the priority for users. Crack smokers' interest about getting safer pipes could suggest their attitude towards their health has a higher priority than simply getting more cocaine. Crack smokers want to share knowledge and information to help their peers. "Every single person commented this is really impressive, really informative good information" said the HR worker in N07. It should be more widely known and used.

This research was the first attempt to use the results of pharmaceutical analysis to inform crack users about risks without any possibility to supply alternative pipes due to legal issues. There needs to be a change in the law in order to get safer equipment to smoke along the same lines as for drug injectors who can obtain clean needles and injecting paraphernalia for free.

Sharing the smoking tools carries infection risks, but the material of the equipment may cause specific health problems, e.g. using plastic equipment which gives off carcinogenic fumes when hot, or sharp glass or tin cans that are associated with inhaling ash or glass shards that may cut lips or fingers. This may show the importance of designing an intervention to increase the knowledge of crack smokers using laboratory results from analysing seized crack samples.

The HR workers proposed assessing more common smoking tools and more varied content within the crack samples, so not only phenacetin or benzocaine as the cutting agent, rather reflecting the situation found in different geographical areas across the country. More diverse results could be used to design more updated and more locally relevant interventions to crack smokers. Optimised interventions could be personalised to make participants feel more important. If this intervention was

designed for them personally, it may encourage them to engage in drugs services and to be more involved in the available and accessible information and services.

The main limitation for this study is supplying participants with information only about the tools they use to smoke crack while it is still illegal to supply them with safer pipes or equipment that could be used to reduce some of the associated problems with the makeshift tools they use currently. Workers commented on some limitations to encourage crack smokers to start taking action towards using safer equipment. The main limitation is that currently in the UK supplying safer pipes is illegal, while supplying clean needles, syringes, and injecting paraphernalia is legal. Although workers valued the importance of increasing the knowledge and awareness of crack smokers to reduce health problems, they emphasized that to gain the desirable actions it is essential to provide safer pipes with the intervention delivery. In August 2014, provision of foil for drug smokers was allowed in the UK, but it is restricted with conditions, e.g. to engage smokers to be involved in a treatment plan or to provide foil as part of a treatment procedure. This is an optimistic step towards more HR procedures to provide safer equipment to smoke drugs that may significantly reduce the dangerous transmission of infectious diseases.

The designed PIPES intervention was mainly aimed at increasing the knowledge of participants towards the efficiency of different smoking tools, cutting agents and their effects, and HR tips for smoking crack. The intervention and the results of the two questionnaires showed the lack of knowledge and communication with this category of drug users. More research into informing them about the dangerous equipment that they use is required. More interventions need to be designed to encourage them to engage with available drugs services so as to reduce their harmful smoking habits. Due to continuous changes in the content of crack samples and tools used to smoke, continuous training and updating of the intervention content is required to keep the participants up to date and engaged in HR services. In conclusion, different analytical methods give different information which together form the analytical profile for unknown crack samples. Profiling could be carried out with fewer methods depending on the availability and ease of interpretation of results. All the techniques used to characterize the differences are available in the Department of Pharmacy and Pharmacology, University of Bath.

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Appendix 1

**Protocol, baseline questionnaire, follow-up questionnaire, intervention, and
guides to deliver the intervention used in these studies**

1. The protocol of the study.



Department of Pharmacy and Pharmacology

Full Research Proposal Template

All researchers involved in this project list team members, roles within project and proportion of the work for which the member is responsible

| Name | Role | % contribution to work |
|-----------------------|-------------|------------------------|
| Mohammad Zaher Shehab | PhD student | |
| Dr Andrea Taylor | Supervisor | |
| Prof Marjorie Weiss | Supervisor | |
| Dr Jenny Scott | Supervisor | |
| Dr Ian Blagbrough | Supervisor | |

Title of the Project

Translating laboratory evidence on the safety of crack cocaine into a harm reduction intervention for use by harm reduction workers.

Summary of the Project View this as an abstract of your intended project

Illicit crack cocaine is usually administered by inhaling the vapour through a makeshift crack pipe. It is commonly adulterated with various compounds. Illicit crack samples have been profiled by different analytical techniques to measure the content of cocaine and adulterants, and a smoking model was optimised to measure the efficiency and recovery of different smoking devices.

The projects aims to translate the findings of the laboratory based work into the practice setting by using the findings as a basis for the design of a short educational intervention. This work will be conducted in close partnership with Bristol Drugs Project (BDP). The study consists of three phases study. Phase one involves co-designing the questionnaire and intervention by running a focus group with harm reduction workers who provide harm reduction services for users in Bristol, and few drug users who are interested in this study. Phase two will entail administering baseline questionnaire to users to measure the in knowledge and awareness crack cocaine smoking and impurities. The educational intervention by harm reduction workers in shelters or hostels where they meet users will then be delivered.

Immediately after the intervention harm reduction workers will measure the knowledge of the users again. A further following up is planned after 2- 3 months, by the harm reduction workers, to measure the knowledge and any change in the users' behaviour. The last step of phase two is to arrange a focus group with harm reduction workers who were involved in the study to optimise and develop educational intervention so it can be used on a larger scale through the mobile service that harm reduction workers provide it to drug users in different areas in Bristol. Phase three will deliver the enhanced harm reduction message via the mobile service to spread the

outcome of the study to larger population. There will be a new short follow up questions immediately after this short intervention.

Lay Person's Summary of the Project (suitable for use by the media)

Avoid the use of highly technical terms. Be brief and describe the overall aims of the research and expected outcomes in a manner the general public will understand.

Keywords/Phrases describing the research and its approach no more than 4 terms.

Crack cocaine smoking

Harm reduction

Adulterants

Educational intervention

Information motivation behaviour model

PROJECT PROTOCOL

Research Question/Hypothesis

What are the effects of an information-based intervention to increase the awareness of the harms associated with crack use and to alter crack users' behaviour?

Background/Introduction Set out the rationale for the piece of research, including a synthesis and analysis of previous research in the same field.

Shrubs of the plant family Erythroxylaceae, namely *Erythroxylum coca* (Bolivian or Huanuco) and *E. truxillense* (Peruvian or truxillo), are the source of coca leaves from which cocaine originates; these trees are grown in Bolivia, Colombia, Peru, and Indonesia[1]. Coca has been used as a traditional drug in South America for thousands of years as a general stimulant or for other limited medical usages[2]. Medical usage of cocaine is described in European medical texts as early as the 17th Century. In the late 19th Century, coca extract and cocaine were prepared as remedies for many problems[3].

Crack cocaine is a free-base form of the illicit drug cocaine that is manufactured by various procedures. It is commonly adulterated with compounds such as phenacetin, benzocaine, glucose, and mannitol.

Smoking crack cocaine causes many pulmonary symptoms e.g. pulmonary oedema, hypersensitivity pneumonitis, pulmonary haemorrhage; other routes of cocaine abuse do not cause these pulmonary problems[4]. Topical application of cocaine to the cornea can cause corneal damage with clouding, pitting, sloughing, and occasionally ulceration. Topical application to the nose or mouth has been reported to cause loss of smell and taste respectively. Long-term use of cocaine by nasal inhalation may cause mucosal damage or perforation of the nasal septum[5]. Cocaine crosses the blood-brain barrier and it accumulates in the central nervous system (CNS); it crosses the placenta and is also found in breast milk.

The cocaine market is huge not only in the United States, but also in Europe where it is estimated to be more than \$37 billion and \$33 billion annually, respectively.

Cocaine is considered the second most problematic prevalent drug after heroin as

judged by harmful health consequences; in terms of trafficking related violence, it is probably the major drug[6].

Harms accompanied with cocaine consumption include overdose, and the dangerous health consequences due to multi-drug use and the presence of harmful adulterants are major concerns where cocaine is consumed. Deaths connected with the use of illicit drugs may result from: suicide, fatal drug overdoses, accidents, deaths among injecting users and from infectious diseases such as HIV and hepatitis C, medical conditions (organ failure due to chronic drug use)[6].

In previous work, street crack samples were analysed and profiled by various analytical methods to identify and quantify the components. In another element of this work, the practice of using crack cocaine in vapour form using home-made crack pipes constructed from readily available items such as drinks cans, bottles, or even medical inhaler outer tubes was investigated. An experimental model of crack cocaine smoking has been devised to mimic this process and enable the recovery and analysis of the compounds actually inhaled.

Cocaine street samples are usually cut by dealers with diluents or/and adulterants. Diluents, pharmacologically inert substances such as sugars, talc, or corn starch, are added to increase the samples' bulk and therefore the dealers' profits. Adulterants, which are pharmacologically active substances, are added by dealers to amplify the wanted effects of the illicit substances or to cut down or remove some of the side-effects.

Cocaine adulterants can be divided into three main categories: local anaesthetics, stimulants, and toxins. The purpose of adding local anaesthetics to cocaine is to simulate the anaesthetic properties of cocaine. Local anaesthetics are considered to be the third most common cocaine adulterant. Stimulants such as caffeine and ephedrine look (to the eye) like cocaine, and are legally available in pharmacies. They stimulate the CNS and enhance catecholamine release as does cocaine. The two main substances in the toxin category are quinine and strychnine. Quinine has been used as an adulterant for both cocaine and heroin although it has cellular poisonous properties, and it is toxic to heart, kidney, and CNS. The strychnine toxic dose is 30-80 mg and it causes death when 100 mg or more are ingested. There are many complications of strychnine intoxication such as lactic acidosis, myoglobinuria, and acute renal failure. In addition, Levamisole was reported in up to 70% of analysed cocaine samples in USA and Europe. In addition, Levamisole is an anti-parasitic agent used to treat colon cancer and rheumatoid arthritis [7, 8].

There has been one previous attempt to evaluate the knowledge of dealers about the components utilised and their awareness of the adulterants and their dangerous consequences[9]. On the other hand, there are many papers published to study the impact of different interventions and methods on users' behaviours [10-12]. Most of these studies rely on affecting motivation in ordering to change behaviour. Other psychological approaches which could be shown to influence behaviour are sorely needed.

There are many interventions designed to study change in behaviour towards a range of habits and activities [13, 14]. In the drug abuse domain, many theories were used to design interventions that were expected to have desirable effects on health users to reduce drug use and raise awareness of sexual practices [11, 12]. To avoid any

individual, cultural and background differences and to encourage users to pay attention to their health, or information intervention may be useful. The focus of this protocol is to use an information-based intervention to study the impact of information on users' behaviours.

There are potential advantages to this intervention in terms of the cost of cocaine consumption over the world and upon the users' health. It could improve the state of health of users by reducing users' risk taking behaviours, and it may decline the violence related to cocaine dealing. Also, it may help the health sector to reduce the cost of treatment and caring for cocaine users due to the expensive cost of the consequences of ingesting either cocaine or hazardous adulterants.

Aim of Research

The aim of this study is to develop an information based-intervention for use by harm reduction workers, aimed at crack cocaine users. This intervention study will design a tool that can help workers to provide crack users with more information and support in order to help to reduce harms associated with crack consumption.

Objectives of Research

- to evaluate via a baseline questionnaire the knowledge and awareness of crack cocaine users about the health problems arising from smoking crack cocaine, specifically as a result of consuming impure samples and using different home-made pipes.
- to design and deliver an information-based intervention based on the information motivation behaviour model (IMB), using the analytical data collected by profiling seized samples.
- to measure any change in drugs users' knowledge and attitudes towards crack cocaine smoking brought about by their involvement in the IMB workshop to develop the intervention.
- to measure whether experiencing the intervention changes knowledge and self-reported behaviour at one/three months post intervention amongst crack cocaine smokers.
- to deliver an information-based intervention to a wider group of hard to reach drug users.

Research Design - Statement of methods Design and methods to be used. Include details of guiding methodology, setting, participants (and intervention if appropriate), recruitment, sampling strategy(ies), data collection method(s), including outcome measures and method of measurement and your approach to data analysis etc as outlined in the guidance notes.

There are three phases in this study.

Phase one:

Co-design a brief educational intervention on crack adulterants.

Intervention: The Bath Education Crack Cocaine Intervention "BECCEI" will be designed in a workshop in partnership with harm reduction workers and service users using the Information Motivation Behaviour model (IMB). The intervention will be short, and will draw on active learning pedagogies to increase user participation. This

way of designing the intervention is being used in order to get the optimal design and to avoid any barriers that could lead to misunderstandings or rejection from the users.

Phase two:

Evaluation of intervention with thirty service users who have an existing and 'stable' relationship with BDP. The recruited crack users will answer a questionnaire then at the same session will participate in the intervention delivered by harm reduction workers. The intervention will include information about adulterants, identified from the laboratory analysis: - the compounds produced during volatilizing the samples (similar to what would be produced during smoking crack); the health problems associated with consuming impure samples; and the problems with using home-made pipes compared with distributed harm-reduction pipes regarding the inhaled dose or the risk of associated infectious diseases.

After the intervention is completed, the participants will be asked to answer a second questionnaire to evaluate their knowledge and awareness of crack adulterants and their harmful effects and, to explore whether the intervention has caused any immediate change in their knowledge, awareness and attitudes regarding crack cocaine use. This questionnaire will follow the first stage of the Kirkpatrick model [15].

After one month, the crack users will be asked to answer a third questionnaire, which is a follow-up step in the study. This will measure the impact of the intervention on their crack cocaine smoking practices and their attitude toward smoking behaviour.

Finally, Harm Reduction workers will be invited to participate in a focus group to analyse the results that are collected from users after the intervention and to reflect on their involvement in the intervention. The data collected from the focus group (along with that from the drug users) will be used to enhance and refine the intervention. participants will be provided with a shopping voucher and red T-shirt (something memorable) to thank them for their participation. The T-shirt will act as a reminder that the client took part in the intervention.

Phase three: (Large scale and short intervention)

A revised version of the intervention will be offered by harm reduction workers to a larger population of drug users via the BDP mobile drug service. This version will be shorter and deliver a focused harm reduction message. Currently the mobile service usually meets 100-200 users a week in Bristol. This group of drug users is historically harder to reach and follow up. This short intervention will be delivered by harm reduction workers during a specified week of operations.

It is ambition three of this phase of the study simply to record how many drug users participated in the intervention and to see if there is mediate change in their knowledge of crack cocaine contaminants.

Outline Project Plan

Diagram for the design and delivering the information-based intervention.

| Time 2013 | Phases | Users | Workers |
|-----------|--------|-------|---------|
|-----------|--------|-------|---------|

| | | | |
|----------|-------|--|-------------|
| July | one | Primary baseline questionnaire | |
| | | Intervention design | |
| August | two | Baseline questionnaire (knowledge & behaviour) | |
| | | Intervention | |
| | | Immediate post intervention questionnaire (knowledge) | |
| October | | Follow-up questionnaire (knowledge & behaviour) | |
| | | | Focus group |
| November | three | Delivering the Harm Reduction message and few questions. | |
| December | | Data analysis | |

Ethical and legal statement What do you believe are the ethical/legal implications of this research?

| |
|---|
| <p>Description of general ethical considerations</p> <p>Informed Consent – all of the participants (drug users and harm reduction workers) will be provided with information about the study and will be invited to participate. The consent form will explain what is required of participants and confirm that they are free to withdraw at any point during the study without mentioning the reasons. Anonymity of participants will be assured.</p> <p>Data Protection all data in this study will be collected and stored in accord with the requirements of the Data Protection Act.</p> <p>Participant Safety - this will be assured through choosing a place where no risk will be possible toward carrying this study due to dealing with vulnerable participants. The harm reduction workers who will deliver the intervention to crack users used to meet the users in hostels and shelters, so they have a good relationship with them. This will facilitate the study and ensure the safety to complete the study without any problems.</p> <p>Competence – only those participants competent to participate in the study will be involved (as determined through advice from the Harm Reduction Workers).</p> |
| <p>Information about any external approval requirements in your practice setting e.g. NHS REC, NHS Research Governance</p> |
| <p>Description of how participants will be informed and consent obtained</p> <p>The posters will announce the study in the centre where the study will be carried out. Information sheet and consent sheet will be signed by users before the study to inform them about the details.</p> |
| <p>Considerations of any problems of confidentiality, information about data storage and data protection arrangements:</p> <p>All data will be stored anonymously.</p> |
| <p>How will data be stored:</p> <p>Anonymously and security- see below</p> |

Information about data protection arrangements:

Data protection: An electronic copy of the audio recordings of the interviews will be stored on a password protected computer. In addition all the paper copies will be locked in cabinet within a number-pad controlled access office within the department. The data will be stored, handled and destroyed in accordance with the requirements of the UK Data Protection Act.

Quantitative data will be analysed by using SPSS software

Qualitative data will be described and analysed by using Nvivo software

The discussion and analysing of data will be done by using both parts of data to be used to give the final results and conclusion about the impact of the delivered educational intervention.

PPI

The NIHR and Research Councils now promote, encourage and increasingly require organisations to demonstrate evidence of PPI in the research they undertake (National Institute for Health Research 2008). Patient and Public involvement (PPI) means that people are active partners in the research process by, for example, advising on a research project, assisting in the design of a project, or in carrying out the research, rather than being the 'subjects' of research.

| | |
|---|---|
| In which aspects of the research process have you actively involved, or will you involve patients, service users, or members of the public? | Please tick all that apply x <input type="checkbox"/> Design of the research x <input type="checkbox"/> Management of the research x <input type="checkbox"/> Undertaking the research x <input type="checkbox"/> Analysis of results x <input type="checkbox"/> Dissemination of findings <input type="checkbox"/> None of the above |
| Give details of patient, service users or public involvement, or if none please justify the absence of involvement. | Social workers and crack users will be involved in the intervention design to choose the understandable way to deliver the materials and information. |

Outcomes and possible implications of study What will be the key outcomes of this research; what are the possible implications of this study in relation to other work?

The key outcomes of this intervention are:

- to raise the awareness of users about the content of crack samples
- to evaluate the impact of the information on users' practice
- to develop an effective approach for delivery of a harm reduction message which can be used more widely

Dissemination What steps will you take to promote the findings of the research that you are planning?

The intervention materials can be developed in future work depending on the feedback from the participants, and we can present the data through YouTube or some short videos on the Internet to deliver it to more people in different places, including different countries. The results of the study will be published in academic journals.

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The proposal must not exceed 5000 words (excluding references and headings and rubrics).

PLEASE ATTACH APPENDICES (These do not form part of the word count).

The deadline for submission of the protocol will be published on Moodle.

2. Ethical approval.

Department for
Health



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20th June 2013

Dear Mohammed,

Full title: Full title of study: Translating laboratory evidence on the safety of crack cocaine into a harm reduction intervention for use by drugs workers

REACH reference number: EP 12/13 73

The Research Ethics Approval Committee for Health (REACH) reviewed the above application at its meeting held on 20th June 2013.

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion of the above research on the basis described in the application form and supporting documentation.

Please inform REACH about any substantial amendments made to the study if they have ethical implications.

Yours Sincerely



Gordon Taylor
Chair of REACH

3. The baseline questionnaire.

Crack Paper Questionnaire (Baseline) 2014

Complete the questionnaire before discussion the intervention “harm reduction information”

Date:.....

| | |
|--------------------------------|------------------------------|
| Respondent number: | Interviewer number |
| Began interview at : | End interview at : |

1. Do you currently use crack?

| | | |
|-----|--|-----------------------------|
| Yes | if yes, when did you start? (ever not just this episode) | |
| No | have you ever used crack? | Yes . if yes, for how long? |
| | | No |

2. How did you first use crack – smoking or injecting?

3. Please tick the box that best describes your current? Crack use

| | More than once a day | Once a day | 2-6 days a week | Weekly | Fortnightly | Monthly | Less than once a month |
|-----------|----------------------|------------|-----------------|--------|-------------|---------|------------------------|
| Smoking | | | | | | | |
| Injecting | | | | | | | |

4. If you smoke AND inject crack how do you decide which method you are going to use?

| | |
|--|--|
| 1. I use the safest method of the two | 2. I have a preferred method |
| 3. I use the most convenient method | 4. I use whatever method those I am using with use |
| 5. I inject if I can get a vein (i.e. vascular access) | 6. Other reason |

5. What do you consider to be the positives and negatives of these two methods?

| | Positives | Negatives |
|-----------|-----------|-----------|
| Smoking | | |
| Injecting | | |

6. How old were you when you first used crack? _____ years (validate Q1)

7. Think back to the first time you used crack. With whom did you first use crack?

| | | | |
|--------|---------------|--------------|---------------|
| Alone | With a friend | With a group | Family member |
| Other: | | | |
| | | | |

8. Think back to when you first used crack, where did you first use crack?

| | | | |
|----------|-------------|--------|--------|
| Own Home | Crack House | Street | Prison |
| Hostel | Youth club | Work | Other |

9. On average how many pipes do YOU get from a single £10 rock? _____

10. How would you describe your pattern of crack use over the last 4 weeks?

I mostly used..... (Follow up)

| | More than once a day | Once a day | 2-6 days a week | Weekly | Fortnightly | Monthly |
|-----------|----------------------|------------|-----------------|--------|-------------|---------|
| Smoking | | | | | | |
| Injecting | | | | | | |

How typical is this pattern of use? _____

11. How old were you when you started using crack regularly? We define regularly as within relatively short intervals e.g. at least every week.
_____ years

12. How do you usually obtain crack?

| | | |
|------------|--------|----------|
| Wash it up | Buy it | Given it |
| Other: | | |

13. What do you use to smoke crack?

| | | | |
|-----------|-----------|------|---------|
| Stem pipe | Ball pipe | Cans | Inhaler |
| Other: | | | |

14. Why do you choose this pipe?

| | | | |
|--------------|----------------|---------------|------|
| Availability | More efficient | Most pleasant | Cost |
| Other: | | | |

15. Can you describe any difficulties you have had as a result of your pipe choice?

16. Have you ever smoked then passed the pipe to another or taken it from another who has previously smoked from it? Y or N
Why

17. What sorts of things do you think crack is cut with?

18. Do you think that crack cutting agents are:-

| | | |
|---------------|-------------------|----------------|
| Never harmful | Sometimes harmful | Always harmful |
|---------------|-------------------|----------------|

19. Do you check the quality of the crack you use? Y/N. If yes.....how do you do this?

| | | | |
|----------|----------|-----------|-----------|
| The look | The feel | The smell | The taste |
| Other: | | | |

20. Do you check quality before you buy? Y/N.

21. If yes, does quality influence your buying decision? Y or N

If yes how?

22. Have any of the following influenced your opinion about crack?

| | | | |
|---------------------|-------------------|----------------|---------------|
| Other users | Non using friends | Family members | Drug services |
| News | Books | Internet | Doctor |
| Personal experience | | Other: | |

23. Over the last two years how often do you think you have engaged with a Drug Treatment Service, to support your crack use? _____

24. If you have engaged with a Drug Service over the last two years for any other drugs please indicate which below.

| | | | |
|--------|-------------|----------|----------|
| Heroin | Amphetamine | Ketamine | Benzos |
| M-cat | Ecstasy | Cannabis | Alcohol |
| Khat | Solvents | GHB | Steroids |
| Other: | | | |

25. If safe glass pipes were available from this service, do you think people would be encouraged to access to drug service more? Y/N
Why?

26. What is your age? _____

27. What is your gender? Male/Female/Other _____

28. Relationship status

| | | |
|-----------|----------|-------------------|
| Single | Married | Civil partnership |
| Separated | Divorced | Widowed |
| Other | | |

29. Employment status

| | | | |
|--------------|--------------|--------------|----------------|
| Employed F/T | Employed P/T | Seeking work | Unable to work |
| Student F/T | Student P/T | Retired | Volunteering |
| Other: | | | |

30. How old were you when you finished school or full time education?

| | |
|---------------------|------------------------|
| 16 years or younger | 17 to 18 years |
| 19 years or older | Still in F/T education |

31. How would you describe your ethnicity/ (tick one)

White:

| | | |
|---------------|-------------|-------------|
| White British | White Irish | White Other |
|---------------|-------------|-------------|

Black:

| | | | |
|---------------|-----------------|---------------|-------------|
| Black British | Black Caribbean | Black African | Black other |
|---------------|-----------------|---------------|-------------|

Asian:

| | | | | |
|---------------|--------|-----------|-------------|-------------|
| Asian British | Indian | Pakistani | Bangladeshi | Asian other |
|---------------|--------|-----------|-------------|-------------|

Mixed:

| | | | |
|-----------------------|---------------------|-------------|-------------|
| White/Black Caribbean | White/Black African | White Asian | Other mixed |
|-----------------------|---------------------|-------------|-------------|

Other:

| | |
|---------|-------|
| Chinese | Other |
|---------|-------|

End with a thank you and debrief

.....STOP.....

4. The follow-up questionnaire.

Follow up questions to be asked 2-4 weeks after the intervention “harm reduction information”

Date:

| | |
|--------------------------------|------------------------------|
| Respondent number: | Interviewer number |
| Began interview at : | End interview at : |

1. Do you currently use crack?

| | | |
|-----|--|-----------------------------|
| Yes | if yes, when did you start? (ever not just this episode) | |
| No | have you ever used crack? | Yes . if yes, for how long? |
| | | No |

2. Please tick the box that best describes your current? Crack use

| | More than once a day | Once a day | 2-6 days a week | Weekly | Fortnightly | Monthly | Less than once a month |
|-----------|----------------------|------------|-----------------|--------|-------------|---------|------------------------|
| Smoking | | | | | | | |
| Injecting | | | | | | | |

3. If you smoke AND inject crack how do you decide which method you are going to use?

| | |
|--|--|
| 1. I use the safest method of the two | 2. I have a preferred method |
| 3. I use the most convenient method | 4. I use whatever method those I am using with use |
| 5. I inject if I can get a vein (i.e. vascular access) | 6. Other reason |

4. What do you consider to be the positives and negatives of these two methods?

| | Positives | Negatives |
|-----------|-----------|-----------|
| Smoking | | |
| Injecting | | |

5. On average how many pipes do YOU get from a single £10 rock? _____

6. How would you describe your pattern of crack use since you were shown the harm reduction information?

I mostly used.....

| | More than once a day | Once a day | 2-6 days a week | Weekly | Fortnightly | Monthly |
|-----------|----------------------|------------|-----------------|--------|-------------|---------|
| Smoking | | | | | | |
| Injecting | | | | | | |

How typical is this pattern of use? _____

7. How do you usually obtain crack?

| | | |
|------------|--------|----------|
| Wash it up | Buy it | Given it |
| Other: | | |

8. What do you use to smoke crack?

| | | | |
|-----------|-----------|------|---------|
| Stem pipe | Ball pipe | Cans | Inhaler |
| Other: | | | |

9. Why do you choose this pipe?

| | | | |
|--------------|----------------|---------------|------|
| Availability | More efficient | Most pleasant | Cost |
| Other: | | | |

10. Can you describe any difficulties you have had as a result of your pipe choice?

11. What sorts of things do you think crack is cut with?

12. Do you think that crack cutting agents are:-

| | | |
|---------------|-------------------|----------------|
| Never harmful | Sometimes harmful | Always harmful |
|---------------|-------------------|----------------|

13. Do you check the quality of the crack you use? Y/N. If yes.....how do you do this?

| | | | |
|----------|----------|-----------|-----------|
| The look | The feel | The smell | The taste |
| Other: | | | |

14. Do you check quality before you buy? Y/N.

15. If yes, does quality influence your buying decision? Y or N

If yes how?

16. Have any of the following influenced your opinion about crack?

| | | | |
|---------------------|-------------------|----------------|---------------|
| Other users | Non using friends | Family members | Drug services |
| News | Books | Internet | Doctor |
| Personal experience | | Other: | |

17. If safe glass were available from this service, do you think people would be encouraged to access to drug service more? Y/N
Why?

End with a thank you and debrief

BDP follow-up questionnaire

Follow up questions to be asked 2-4 weeks after the intervention “harm reduction information”

Date:

| | |
|--------------------|--------------------|
| Respondent number: | Interviewer number |
|--------------------|--------------------|

1. How would you describe your pattern of crack use over the last... weeks?

| | More than once a day | Once a day | 2-6 days a week | Weekly | Fortnightly | Monthly |
|-----------|----------------------|------------|-----------------|--------|-------------|---------|
| Smoking | | | | | | |
| Injecting | | | | | | |

2. A) What do you use to smoke crack over the last... weeks??

| | | | |
|-----------|-----------|------|---------|
| Stem pipe | Ball pipe | Cans | Inhaler |
| Other: | | | |

B) Has this changed since your first intervention?

3. Have you shared or spoken about any of the information in your first interview with anyone else?

Can you remember what information it was you shared?

4. Can you remember how you used/ intend to use the vouchers you were given for participation in the study?

5. The PIPES intervention.

Promoting Inhaled Pleasure Easily and Safely

| Device | Risks | Dose |
|---------|---|------|
| CANS | Burning, cutting lips. Risk of HIV, Hepatitis C | 31% |
| INHALER | Cancer risk from plastic | 47% |
| SHOOTER | Safest Option | 39% |



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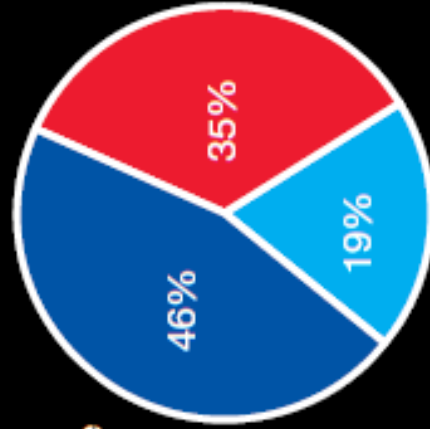
Promoting Inhaled Pleasure Easily and Safely

Harm Reduction Tips

- 1 Never share any of your smoking equipment
- 2 Avoid alcohol when using crack
- 3 Take regular long breaks and decide the maximum you're going to use before you start and stick to it
- 4 Drink enough water and look after your lips

Cocaine percentage in crack samples

- Cocaine
- Phenacetin
- Cutting materials



Phenacetin

- Hurts your kidneys
- Damages your liver



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6. Guideline to deliver the intervention to crack smokers

Please show the person the 'PIPES' A4 information card. Please discuss with them in the following order:

- The amount of crack we measured that each pipe delivers to the lungs (first page with pictures of hands and pipes). The % of crack is shown in the top right corner of the picture.
- The inhaler delivers a higher dose but we are concerned about plastic from the device being harmful if heated up and residue is breathed in. How does the participant view this information in terms of choice of pipe?
- Do they think crack users would use the safer glass shooter knowing the dose could be less?
- Would this info encourage them to use inhalers over cans even though they may be risker?

Now turn over the advice card.

- Please discuss the 4 harm reduction tips that are listed. Are there any barriers to following this advice in real life?

Finally, please show the person the circle 'pie' chart with the percentage content of crack we analysed. We found 46% was cocaine. 35% was phenacetin which can damage kidneys and has been linked with kidney cancer. 19% was other cutting materials that are less harmful (like sugars).

- Do they think this information would influence crack users on their use of crack? If yes, how? If no, why not?
- Does the person have any suggestions for what could be done to make crack use safer (e.g. supply of safer pipes that are as effective as inhaler pipes?)

End.

Please give the person a shopping voucher. Ask them to sign the receipt log which has to be returned to the University of Bath. They can initial this, to avoid any names being used.

Debrief – if person would like to discuss any of the issues raised by the questionnaire please raise them with Lee who can refer any questions back to the University of Bath.

Appendix 2

Poster and Oral Abstracts presented from these studies

1- IHRA, 2011.

The potential of “raw” output from analytical techniques to enhance harm reduction advice to users of crack cocaine

M. Zaher Shehab, Michael G. Rowan, Ian S. Blagbrough, and Jenny Scott
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The aim of our research is to establish that profiling illicit crack cocaine samples can make a contribution to reducing the associated harm to the health of users.

Different cutting agents are used to increase the bulk of cocaine samples, some agents mimic the properties of cocaine, but mainly they are cheap and readily obtainable. However, the cutting agent can be harmful to health, e.g. phenacetin causes renal damage. Quantifying the ratios of cocaine to impurities, in a collaboration with a drugs service and the police, may contribute to solving some of the many problems from which addicted users suffer.

Samples of crack cocaine seized by police in Swindon, UK, were examined by a range of analytical methods: high performance liquid chromatography (HPLC), high performance thin layer chromatography (HPTLC), gas liquid chromatography (GLC), nuclear magnetic resonance (NMR) and infra-red (IR) spectroscopy, and mass spectrometry (MS). In addition to quantifying the cocaine content and identifying and quantifying the major contaminants, a full profile of the chemical composition of illicit cocaine samples may be of value in tracking the samples' origin and in predicting adverse effects, thus yielding precautionary measures to decrease the harm resulting from the impurities.

HPLC analysis of these samples showed that cocaine content varied from 4% to 80% with a mean of around 40%. NMR analysis showed that phenacetin was present in about 80% of samples; other contaminants identified were benzocaine, glucose and mannitol. NMR spectroscopy, IR spectroscopy, MS and HPTLC all provide visual bar-code-like fingerprints that can be incorporated into local harm reduction messages that may be useful in conveying an impression of contamination to drug service personnel or to drug users, reinforcing the message and leading to harm reduction.

We thank the Government of Syria through Damascus University for financial support of this work (fully-funded PhD to MZS).

Differential Scanning Calorimetry of Street Samples of Crack Cocaine

M. Z. Shehab, I. S. Blagbrough, R. Price, M. G. Rowan, J. Scott
Department of Pharmacy, University of Bath, Bath, UK.

Abstract – Illicit crack cocaine is usually taken by inhaling the vapour through a makeshift crack pipe. The thermal behaviour of pure cocaine and crack cocaine was studied to determine the appropriate temperature for the operation of different kinds of crack pipes. Street samples of crack cocaine gave complex thermal profiles that may prove useful in differentiate of different illicit sources. All showed endothermic peaks below 100° for melting of the cocaine base, which suggests a suitable crack pipe operation temperature of about 100°.

INTRODUCTION

Crack cocaine is a free base form of the illicit drug cocaine that is manufactured by various makeshift methods. Users take the drug in vapour form using home-made 'crack pipe' devices constructed from readily available items such as drinks cans, bottles and medical inhalers[1]. Some drugs services provide standardised pipes as a harm reduction measure due to concerns that shared pipes may transmit hepatitis C virus and to attract users into services.

In an attempt to devise an experimental model of the crack smoking process, a DSC study of cocaine, street samples of crack cocaine and its common adulterants was undertaken. A previous DSC study [2] of cocaine HCl and adulterants commonly used in the late 1980s focused on the use of DSC as a method for the analysis of seized samples. This is the first study of the thermal properties of cocaine base and modern adulterants carried out in order to understand the processes that occur during the smoking of crack cocaine.

MATERIALS AND METHODS

Crack cocaine was seized by Police in Swindon, UK. DSC (DSC 2920 TA instrument, 30 L/min N₂, 10°C/min, 50-275°C). NMR analysis used a Bruker Avance for qualitative identification of cocaine and adulterants (1H at 400 MHz, d₆DMSO). HPLC with UV/VIS detector Perkin Elmer (Shelton, USA) for quantitative determination of cocaine and adulterants (Column: 150x 4.60 mm, Gemini 5µ C18 110A maintained at 35°C. Mobile phase: H₂O: Acetonitrile: THF: triethylamine (580:360:60:0.5 v/v/v/v). Detection: UV/Vis (λ = 249 nm (0-4 min), 297 nm (4-9 min), 233 nm (9-11 min)).

RESULTS AND DISCUSSION

DSC scans of pure samples of cocaine HCl, cocaine base, phenacetin, benzocaine and glucose were produced. All showed the expected endothermic and exothermic peaks for melting, followed in some cases by evidence of thermal decomposition (Figure 1). DSC scans of the street samples of crack cocaine generally showed a slight depression in the transition temperature of both cocaine base and the main adulterant (Figure 2).

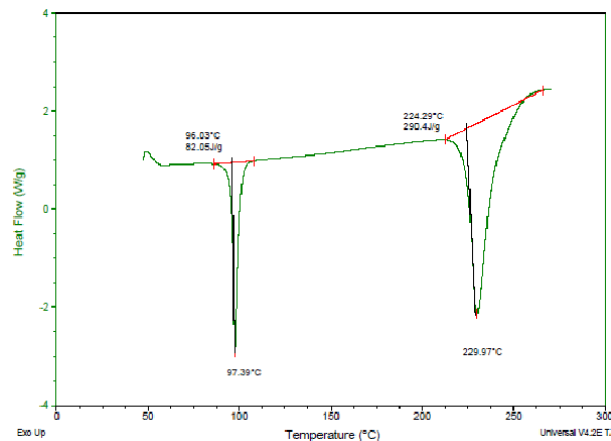


Fig. 1. Thermal graph of cocaine base.

Moreover, the scans also showed other complex features maybe related to other minor components in the mixtures or possible chemical reactions between components.

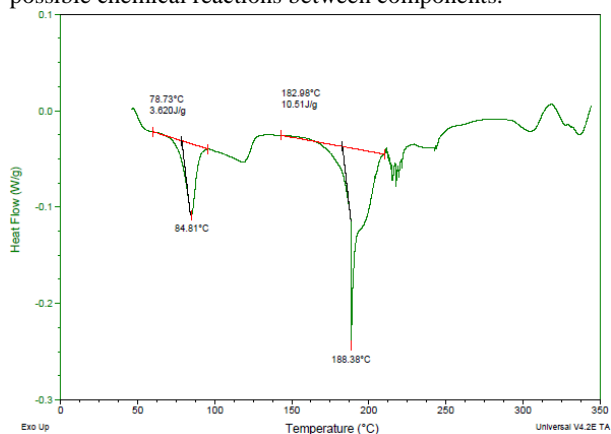


Fig. 2. Thermal graph of crack sample containing cocaine and phenacetin.

CONCLUSIONS

Different street samples of crack cocaine gave markedly different DSC profiles, and it is likely that this influences the performance of the crack during use. It is intended to use these data to devise an experimental model of the process of crack smoking to evaluate the performance of various types of crack pipe with a long-term view of informing suitable harm reduction interventions.

ACKNOWLEDGMENTS

(MZS thanks the University of Bath for financial support)

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An Experimental Model of Crack Cocaine Smoking

M. Z. Shehab, I. S. Blagbrough, R. Price, M. G. Rowan, J. Scott

Department of Pharmacy, University of Bath, Bath, UK.

Abstract – Illicit crack cocaine is usually taken by inhaling the vapour through a makeshift crack pipe. The efficiency of this means of administration and the effects of heating on the cocaine base and adulterants in the crack are unknown. Thus, an experimental model of crack cocaine smoking has been devised and used to investigate the vapour likely to be inhaled from a street sample of crack. Approximately 37% of the cocaine base and 47% of the phenacetin adulterant in this sample was recovered from the vapour.

INTRODUCTION

Crack cocaine is a free base form of the illicit drug cocaine that is manufactured by various procedures. It is commonly adulterated with compounds such as phenacetin, benzocaine, glucose and mannitol [1]. Crack cocaine is taken in vapour form using home-made crack pipes constructed from readily available items such as drinks cans and bottles and medical inhalers. Some drugs services supply standardised pipes as a harm reduction measure [2].

The whole procedure of crack manufacture, adulteration and delivery via a thermal process provides many opportunities for chemical degradation and modification of both cocaine and adulterants. Although previous studies have evaluated the thermal stability and thermal degradation products of cocaine[3], no previous attempt has been made to determine what chemicals are delivered to the users' lungs.

An experimental model of crack cocaine smoking has been devised to mimic this process and enable the recovery and analysis of the compounds actually inhaled.

MATERIALS AND METHODS

Crack cocaine samples seized by police in Swindon, UK were analysed by HPLC to determine cocaine content and by NMR spectroscopy to identify the major adulterants.

Following advice from (drug service personnel), an experimental set-up to mimic the process of crack smoking was devised. This comprised: a pump (GE G626X, USA) set to deliver an air flow rate of 30 L/min; three cold traps (-25 °C) in series; an ACI (Andersen Cascade Impactor) with two stages to collect particles of 4.7µ and 1.1µ respectively; a connection to a customised mouthpiece. For preliminary experiments the mouthpiece was customised to a standardised crack pipe of a type known as a "Canadian Shooter".

After loading, the pipe was carefully heated with a micro burner and the temperature monitored by a temperature probe (TENMA 72-2065, OHIO). An air flow of 30 L/min was established through the pipe and maintained for 10 mins. After this time the airflow was stopped and compounds recovered from the pipe, traps and internal surfaces of the apparatus by dissolution in methanol.

These solutions were analysed by HPLC (Column: 150x 4.60 mm, Gemini 5µ C18 110A maintained at 35°C. Mobile phase: H₂O: Acetonitrile: THF: triethylamine (580:360:60:0.5 v/v/v/v). Detection: UV/Vis (λ= 249 nm (0-4 min), 297 nm (4-9 min), 233 nm (9-11 min)).

The method was optimised using pure cocaine base and then a sample of street crack cocaine containing phenacetin as its main adulterant was examined using the same procedure. Three replicates over which the measured temperature fell within the range 90–130⁰ were carried out.

RESULTS AND DISCUSSION

The crack cocaine street sample contained 45.9 % cocaine, 34.6 % phenacetin plus other unknown constituents probably including inorganic salts such as NaCl and NaHCO₃. Using optimum conditions, three replicates yielded an average recovery of cocaine of 37.0% (s.d. 8.7) as vapour and only 0.9% as particles and a residue in the pipe of 2.4%. For phenacetin, 47.3% (s.d. 12.8) was recovered as vapour with 2.7% as particles and a residue of 3.2% in the pipe.

CONCLUSIONS

This experimental model will be used to compare the performance of other types of crack pipe and to evaluate the chemical composition of the mixture delivered to the lungs from other street crack samples with different adulterants. However, it is already clear from this preliminary study that the commonly adulterant, phenacetin, is efficiently delivered. The pharmacokinetic properties, metabolism and toxicity of orally administered phenacetin are well known [4], but there is little or no information relating to a pulmonary route of administration.

ACKNOWLEDGMENTS

(MZS thanks the University of Bath for financial support)

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4- LTG, 2013.

Tracking crack cocaine samples sources by using principle component analysis

M. Z. Shehab, I. S. Blagbrough, M. G. Rowan, J. Scott
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Abstract – Tracking sources of crack samples can help the police to find the dealers who distribute these poisons in the community. Various analytical techniques and statistical methods could be used to achieve this purpose. Principle component analysis applied on the NMR scans for seized crack cocaine samples in attempt to gather the similar samples which contain same cutting agents (adulterants, diluents).

INTRODUCTION

Principle component analysis provides information about various samples by gathering samples into clusters which have similar components[1]. Seized crack samples were analysed by NMR technique as sensitive, economic, not complicated method to scan unknown content samples of illicit drugs [2-4]. The Crack samples include many adulterants that are added by dealers for different purposes. Same dealers usually use cutting agents depending on availability, drug form, and unknown reasons. This method may help to gather the varied samples into groups that include similar adulterants which were added by same dealer probably.

The aim of this study is to help the police to detect the routes of distribution by following the samples which have same adulterants in one or more area. This may be the first step to establish a data-base contain the information about the purity and adulterants across the country.

MATERIALS AND METHODS

Cocaine hydrochloride, Phenacetin and Benzocaine BP were purchased from Ferris & Co., Bristol, UK, BDH Chemicals, UK, J. M. Loveridge, UK; respectively. Deuterium oxide, deuteriated methanol, and deuteriated chloroform, and deuteriated Dimethyl sulfoxide d6-DMSO were purchased from Sigma-Aldrich, UK.

NMR analysis was using a Bruker Avance (1H at 400 MHz). ¹H NMR analysis was carried out by dissolving crack (10 mg) in d6-DMSO (0.5 mL). Samples were analyzed using a 400 MHz NMR spectrometer. Mnova 8.1.1 software for processing, analysis NMR scans. IBM SPSS statistics 20 is to carry on the PCA technique.

RESULTS AND DISCUSSION

PCA was applied for the NMR data. The result was one cluster because most of the samples contain the same component and in nearly same ratio. For that, another new group of seized samples was provided recently, and they have been profiling. PCA will be carried on these new samples to present the efficacy of PCA to differentiate between varied samples to gather similar samples together.

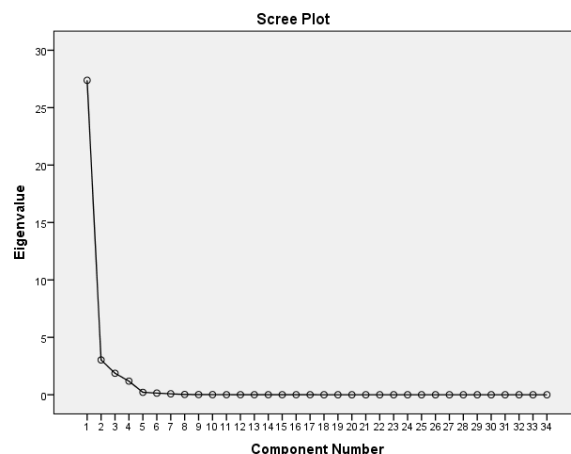


Fig. 1. The Scree plot of PCA results.

The scree plot presents the PCA results so that the most samples were gathered as one cluster because they may be came from one source (Fig. 1).

CONCLUSIONS

Tracking illicit drug samples is an application of pharmaceutical analysis that can provide the police with important evidence how the samples distributed and where the cutting is done at which level. PCA and other statistical methods are used relying on natural minor components or adulterants to detect the geographical or source of these drugs around the world [5].

ACKNOWLEDGMENTS

We thank the University of Bath, Wellcome Trust, and Said Foundation for financial support for MZS

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